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RESEARCH ARTICLE

COMPARISON OF EFFECTIVENESS OF SPUTUM CYTOLOGY WITH BRONCHOALVEOLAR LAVAGE (BAL) IN THE DIAGNOSIS OF LUNG CANCER

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ABSTRACT

Sputum cytology is a simple, accurate, reliable, cost effective and non-invasive procedure for the diagnosis of pulmonary lesions including preinvasive and invasive malignancies. BAL (Bronchoalveolar lavage) is a valuable diagnostic and research tool in pulmonology.

Aims: To compare the efficacy of Sputum cytology with BAL in the diagnosis of lung cancer.

Material and Methods: 2 year study was carried out. Sputum cytology, BAL and bronchoscopic biopsies were done in 97 cases. Comparison of effectiveness of Sputum cytology and BAL in diagnosing lung cancer is done with 'z' test.

Results: Total 97 cases were included in the study, 33 cases were positive for malignancy. Sensitivity of sputum cytology and BAL were 30% and 69.6% respectively. On applying 'z' test for statistical analysis p value of <0.0001 is obtained. Hence we conclude that there is a significant difference in proportions between sputum cytology and BAL in diagnosing lung cancer. So BAL is more effective diagnostic modality for lung cancer in comparison to sputum cytology.

Conclusion: BAL cytology is significantly more effective in the diagnosis of lung cancer in comparison to sputum cytology. As sputum cytology is a simple, reliable, cost effective and non-invasive procedure it can still be used as one of the diagnostic modality for lung cancer with fairly good sensitivity.

INTRODUCTION

Sputum cytology is an example of exfoliative cytology, which is based on the exfoliation of cells from the lining of the organ into a cavity from which cells can be obtained by a non-invasive means. (Myron *et al.,* 2009) It is a simple, accurate, reliable, cost effective and non-invasive procedure for the diagnosis of pulmonary lesions including preinvasive and invasive malignancies. (Roby *et al.,* 1990; Gupta and Garg 2006) Bronchoalveolar Lavage (BAL), which was initially developed as therapeutic tool has also gained acceptance and popularity as a tool for the diagnosis of lung cancer. (Gaur *et al.,* 2007) Our aim was to study and compare the efficacy of Sputum cytology with BAL in the diagnosis of lung cancer by correlating them with histopathological diagnosis by bronchial biopsy

MATERIALS AND METHODS

The study was carried out in the department of Pathology at ESICMCPGIMSR, Bangalore. Out of all clinically and radiologically suspected cases of lung cancer received from June 2010-june 2012(two years), i.e. 107, we selected 97 cases where sputum cytology, BAL and bronchoscopic biopsy were available. The case was not included when any one of the three samples are inadequate.

Histopathological diagnosis by bronchial biopsy was considered as gold standard. (Gaur *et al.,* 2007) A fresh early morning sputum sample produced by deep cough was collected in a wide mouthed, shallow, sterile glass or plastic container for three consecutive days. The container was properly labelled and sealed with tight fitting lid. Four smears were made of each sample and stained with H&E, Papanicolaou, Leishmann and May Grunwald Giemsa (MGG) stains. Samples were regarded as satisfactory if alveolar macrophages were present. (Khalid *et al.,* 2010) All slides were examined under microscope for malignant cells. BAL samples were obtained by flexible fiber-optic bronchoscopy done by the Pulmonologist. Samples were received in 20ml aliquots of normal saline in sterile vials. (Gaur *et al.,* 2007) Samples were centrifuged and smears prepared with the sediment. Four smears were made and stained like that of sputum and were examined under microscope for malignant cells. The bronchoscopic biopsy was processed in an automated tissue processor and paraffin blocks were made. From each block three sections were taken at different levels and stained with H&E stain. Immunohistochemistry was done wherever required for confirmation. (Khalid *et al.,* 2010) 'z' test of statistical significance was applied to compare the

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effectiveness of Sputum Cytology with BAL in the diagnosis of lung cancer.

RESULTS

The study included 97 patients with clinically suspected lung cancer. Of these, 33 cases were subsequently confirmed as lung cancer by histopathologic evidence. Thus we have 33 confirmed cases of lung cancer in the present study. Out of 97 patients 79 were male and 18 were female with their age ranging from 50-79 years. The male: female ratio was 4.3:1. Age of the confirmed lung cancer patients were ranging from 50 to 72 years with mean of 60.8 years. A history of smoking more than fifteen cigarettes per day for longer than five years was given by 32 cancer patients. We thus have a striking majority of 96% smokers in cancer patients group. Sputum was positive for malignant cells in 10 cases (30%) and BAL cytology was positive in 23 cases (69.6%). There were no false positive cases. Distribution of different types of lung cancers and the percentage of positivity in each modality is described in Table 1 & 2. Radiological and bronchoscopic studies revealed a central or perihilar tumors in 11 cases of which 8 were positive for malignancy on sputum cytology giving a pick up rate of 72.7% for central lesions compared to 9% (2 cases) of 22 peripheral lesions. Thus in these 33 cases the following observations were made, Sensitivity of sputum cytology- 30% Sensitivity of BAL cytology- 69.6% on applying 'z' test, p value of <0.0001was obtained. Hence we conclude that a significant difference in proportions is there in between sputum cytology and BAL cytology. So BAL cytology is more effective diagnostic modality in comparison with sputum cytology in the diagnosis of lung cancer.

Table 1. Distribution of different types of lung cancer

	Number of cases	%
Squamous cell carcinoma.	20	60.6
Adenocarcinoma.	07	21.2
Small cell carcinoma.	02	06.06
Large cell carcinoma.	01	03
Neuroendocrine tumor.	01	03
Lymphoma	01	03
Plasmacytoma	01	03
Total	33	

Table 2. comparison of effectiveness of BAL and Sputum cytology in different types of lung cancers

	BAL* cytology	Sputum cytology	Biopsy
Squamous cell carcinoma.	13	08	20
Adenocarcinoma.	07	02	07
Small cell carcinoma.	01	00	02
Large cell carcinoma.	00	00	01
Neuroendocrine tumor.	01	00	01
Lymphoma	00	00	01
Plasmacytoma	01	00	01
Total	23(69.6%)	10(30%)	33

*Bronchoalveolar lavage

DISCUSSION

Lung cancer is an epidemic disease. Increasing evidence suggests that the screening and early detection may improve outcome in lung cancer. (Chaudhary *et al.,* 2010) Sputum cytology is a definite diagnostic test for lung cancer. (Jay *et al.,* 1980) Cytological examination of Papanicolaou stain of sputum is accepted as a useful diagnostic tool in lung cancer. (Ammanagi *et al.,* 2012) In the present study sputum sample spontaneously produced by deep cough were brought without any fixatives. As delay in processing may lead to cellular degeneration, smears were prepared and examined as soon as possible. (Chaudhary *et al.,* 2010; Thunnissen 2003; Tsang *et al.,*1992; Neumann *et al.,* 2009; Oswald *et al.,* 1975) However Koss has suggested that the specimens with high mucin content like sputum can be preserved for 12-24 hours under refrigeration. (Myron *et al.,* 2009) Advent of flexible fiber-optic bronchoscope has lead to new turn as samples like bronchial washing, BAL and transbronchial biopsy could be collected from the respiratory tract. (Ahmed and Ahmed 2004) BAL is a valuable diagnostic and research tool in pulmonology. (Kopinski *et al.,* 2000) In a comparative study of BAL and open lung biopsy Yamamoto found that the results of these two to have a parallel relation except in few cases. (Yamamoto 1994)

In the present study the age of the confirmed lung cancer patients were ranging from 50 to 72 years with mean of 60.8 years. 32 (96%) patients were smoker. In our study we noted that BAL cytology has high sensitivity of 69.6% in comparison to sputum cytology with 30% sensitivity, showing its superiority in the diagnosis of lung cancer. (Table-3) Sensitivity of BAL in our study is comparable to that of other studies such as, Jay *et al.* (1980) - 63%, (9) Sing A - 50% (Sing *et al.,* 1997) and Gaur D S -39.4%. (Gaur *et al.,* 2007) Sensitivity of sputum cytology in our study was 30%, which was comparable to the studies such as (Choi *et al.,* 2008) with 31.6%, [17] Sing A with 40% (Sing *et al.,*1997) and Khalid M with 45.3% sensitivity. (Khalid *et al.,* 2010)

There were no false positive cases in the present study. If cytology is suspicious or positive for malignancy, repeat cytology and clinical correlation with bronchoscopic and radiological findings is necessary. (Khalid *et al.,* 2010) In the present study majority of the cases were of squamous cell carcinoma followed by adenocarcinoma and other types. Squamous cell carcinoma which is more frequently located in proximal bronchus showed positivity in thirteen cases in BAL cytology and eight cases by sputum cytology. Wongsurakiat *et al.* (1998) found that the diagnostic yield of BAL is influenced by the size and segmental location of the lesion. (Wongsurakiat *et al.,* 1998) In our study radiologic and bronchoscopic studies revealed a central or perihilar tumors in 11 cases of which 8 were positive for malignancy on sputum cytology giving a pick up rate of 72.7% for central lesions compared to 9% (2 cases) of 22 peripheral lesions. These pick up rates are comparable to 85% as reported by Sing *et al.* (1997), 91% as reported by Khalid *et al.* (2010) and 71% as reported by Ammanagi *et al.* (2012) for perihilar tumors. A suspected case of small cell carcinoma of lung in BAL cytology was subsequently confirmed by Immunohistochemistry (chromogrannin and synaptophysin) on bronchoscopic biopsy.

With fairly good sensitivity BAL promises to be a convenient cytological technique that can be confidently utilised for screening of doubtful cases and early diagnosis of lung cancer as it saves the time needed for the processing of the biopsy specimens.

Conclusion

BAL cytology is significantly more effective in the diagnosis of lung cancer in comparison to sputum cytology. As sputum cytology is a simple, reliable, cost effective and non-invasive procedure it can still be used as one of the diagnostic modality for lung cancer with fairly good sensitivity.

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