Published online: 2019-09-26

Original Article

Randomized controlled trial of comparison of the adequacy, and diagnostic yield of endoscopic ultrasound guided fine needle aspiration with and without a stylet in Indian patients: A prospective single blind study

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Abstract

Background: Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is done using EUS-FNA needle with an internal stylet by most of the endosonographers. There is no data to suggest that it improves the quality of cytology specimen, and it is tedious and time-consuming. **Aim:** To compare EUS-FNA specimens obtained with stylet and without stylet for adequacy of the specimen, amount of blood on the slide, number of passes and diagnostic yield. **Materials and Methods:** Patients undergoing EUS-FNA of solid lesions by one experienced endosonographer at an Indian tertiary center from October 2013 to July 2014 were included. Totally, 115 consecutive patients with 128 lesions were randomized to undergo EUS-FNA with or without stylet. Cytology slides were evaluated by a single pathologist blinded to FNA technique. **Results:** EUS-FNA was done with stylet in 66 lesions (Group 1) and without stylet in 62 lesions (Group 2). Site of lesion was lymph node in 67 (52.3%), pancreas in 43 (33.6%), liver in 8 (6.2%), gastrointestinal subepithelial lesion in 4 (3.1%) and others in 6 (4.9%). The average size of the lesion was 23.7 ± 14.8. When outcomes of two groups were compared, there was no statistically significant difference in adequacy of smears ($P = 1.00$), amount of blood on slides ($P = 0.92$), number of passes ($P = 0.49$) and diagnostic yield ($P = 0.86$). **Conclusions:** There was no significant difference in adequacy of the specimen, amount of blood on the slide, number of passes and diagnostic yield between with and without a stylet groups. The use of a stylet does not confer any advantage during EUS-FNA.

Key words Endoscopic ultrasound, fine needle aspiration, stylet

Introduction

Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is a simple and safe modality for the diagnosis of lesions of mediastinum, gastrointestinal tract, and other adjacent tissues. EUS–FNA provides tissue for histological confirmation of the lesions besides accurately describing morphological features.[1-4] The diagnostic yield of EUS–FNA is around 80–90% even when other diagnostic modalities like computed tomography fail.[5] Various factors have been suggested and studied to affect or improve the quality, accuracy and diagnostic yield of EUS-FNA specimens. These include skill and experience of endosonographer and cytopathologist, characteristics of lesion (site, size, and hardness), type and diameter of the needle, number of passes and application of suction; and immediate cytological examination by the onsite cytopathologist.[6-9]

Access this article online

Website: www.jdeonline.in

DOI: 10.4103/0976-5042.150662

Quick Response Code

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All commercially available EUS-FNA systems include a removable stylet and currently, the usual practice is to carry out EUS-FNA with an internal stylet in the lumen of the EUS-FNA needle, reinserting it before each pass. It is felt that the stylet prevents blockage or contamination of the needle with surrounding non-lesional tissue. Use of stylet is thought to improve the quality of specimens and hence enhance the diagnostic yield of specimens obtained. Although this is a logical assumption, there are no data demonstrating that the use of a stylet increases the diagnostic yield or improves the quality of specimens obtained by EUS-FNA.[10] The use of a stylet during EUS-FNA increases the procedure time and chances of needle stick injuries. There are studies from the west comparing EUS-FNA with and without stylet, but there is no data from Indian subcontinent.[11,12]

So, the aim of this study was to compare EUS-FNA specimens obtained with stylet and without stylet for adequacy of specimen, amount of blood on slide, number of passes required and diagnostic yield for benign and malignant lesions.

Materials and Methods

Study design

It was a single blind prospective randomized controlled study. Consecutive patients were randomized into two groups: those undergoing EUS-FNA with stylet (S^+ group) and without stylet (S^- group). A single experienced endosonographer performed EUS-FNA, and all the slides were evaluated by a single cytopathologist who was blinded to the study groups.

Patients and data collection

This study was conducted in the Gastroenterology Department of a Tertiary Care Center in India. All the patients undergoing EUS-FNA for solid lesions were prospectively enrolled for this study from October 2013 to July 2014. This study was approved by ethics committee of the institute. The inclusion criteria were age older than 18 years, ability to provide informed consent, and the presence of a solid lesion of mediastinum, abdomen or gastrointestinal tract.

The exclusion criteria were severe coagulopathy (international normalized ratio >1.5), thrombocytopenia (platelet count <50,000) and inability to sample the lesion because of the presence of intervening blood vessels. The lesions were also not sampled when the results of EUS-FNA would not affect the patient management.

Data were collected regarding patient demography, site and size of the lesion, number of needle passes, use of stylet during EUS-FNA, adequacy of smears, amount of blood in the specimen and final diagnosis of the lesion.

Endoscopic ultrasound guided fine needle aspiration procedure and cytopathology

All EUS-FNA procedures were carried out using a linear Olympus GF-UCT180 echoendoscope (Olympus America Inc., Center Valley, PA, USA). The procedures were performed in the left lateral position under conscious sedation with midazolam and pentazocine. After localizing the lesion, a 22 gauge needle (ECHO-1-22, Cook Medical, Winston-Salem, NC) was used for EUS-FNA. A single size needle was chosen for all lesions to remove the heterogeneity due to variation of needle size. In the S^+ group procedures, the stylet was removed once the needle was in the lesion and reinserted before each pass, whereas in the S^- procedures, the stylet was removed from the needle before inserting the needle into the echoendoscope operating channel and was never used at any time during the EUS-FNA procedure. Totally, 10–12 to-and-fro movements were made during every pass, fanning was done, and suction was used with 10 ml syringe for 2–4 s. All these techniques were similarly applied to both the groups to avoid any technique bias. After each pass, the needle content was spread on glass slides using 10 ml syringe to apply pressure. All slides were fixed with ethanol and sent for examination to a single experienced cytopathologist. After staining with Hematoxylin and Eosin stain, the cytopathologist assessed samples for adequacy (adequate/not adequate), amount of blood on the slide (mild, moderate and severe) and reported the final diagnosis (benign, malignant, suspicious of malignant or inability to make diagnosis due to inadequate specimen).

Statistical analysis

Results for continuous variables were expressed as means and standard deviations. Categorical variables were expressed as frequencies and percentages. The Chi-squared test or Fisher Test was used to compare the qualitative data whereas continuous variables were compared using Student's *t*-test. A two-tailed $P < 0.05$ was considered statistically significant. The GraphPad Prism version 5.03 (GraphPad Software, Inc.,USA) used for statistical analysis.

Results

Totally, 119 patients with 132 lesions were assessed for this study. Out of these, four patients were excluded (two with platelet count <50,000, one with INR >1.5 and one not providing consent). Finally, 115 patients with 128 lesions were included in the study and randomized to undergo EUS-FNA with (S^+ group) or without a stylet (S^- group). The lesion sites included pancreas in 43 (33.6%), mediastinal lymph nodes in 39 (30.5%), abdominal lymph nodes in 28 (21.9%), liver in 8 (6.2%), gastrointestinal subepithelial lesion in 4 (3.1%) and others in 6 (4.7%) patients.

Of these, stylet was used in 66 (51.6%) patients (S^+ group), and sixty-two (48.4%) patients underwent EUS-FNA without a stylet (S^- group). The baseline characteristics of these

two groups are shown in Table 1. Though the mean age of the patients in S+ group (51.9 ± 12.5 years) was less than S-(56.8 ± 16.8 years), the difference was not statistically significant (P = 0.06). Forty (60.6%) patients in S^+ and 41 (66%) patients in S^- group were males. The mean size of the lesion in S^+ group was 24.6 ± 14.2 mm and in S^- group was 22.8 ± 15.1 (P = 0.48). Both the groups were also comparable for the site of lesion.

There was no significant difference in sample adequacy (P = 1.00), amount of blood on the slide (P = 0.92) and number of passes (P = 0.49) between S^+ and S^- groups [Table 2]. The final cytological diagnosis reported in S^+ group was: A benign pathology in 29 (43.9%), malignant in 27 (40.9%), suspicious of malignancy in 3 (4.6%) and inadequate material in 7 (10.6%). In S^- group final diagnosis was: Benign pathology in 26 (41.9%), malignant in 24 (38.7%), suspicious of malignancy in 3 (8.1%) and inadequate material in 7 (11.3%). When the final diagnostic yield was compared between the two groups, there was no statistically significant difference (P = 0.86).

Because the site of the lesion is one of the factors that affect sample adequacy and diagnostic yield,[13] we compared the data of lymph node and pancreatic lesions, which constituted majority of the lesions (52.3% and 33.5% respectively) [Table 3]. There was no statistically significant difference in sample adequacy (P = 1.0), number of passes (P = 0.63) and diagnostic yield (P = 0.75) for lymph node lesions. Similarly when data from pancreatic lesions was analyzed, there was no statistically significant difference in sample adequacy (P = 0.65), number of passes (P = 0.76) and diagnostic yield (P = 0.97). To make data values valid, suspicious of malignancy, and inadequate samples were used as combined value while comparing the diagnostic yield in pancreatic lesions.

Discussion

Endoscopic ultrasound guided fine needle aspiration has revolutionalized the diagnosis of various mediastinal and abdominal lesions that earlier used to be inaccessible with conventional diagnostic techniques. Moreover by providing the tissue for diagnosis, it has helped in differentiating benign from malignant lesions that altogether have different course and management. The stylet is used by most of the endosonographers despite the lack of any evidence supporting its use. This use is based on the thought that reinsertion of stylet after each pass prevents clogging of the needle with normal gastrointestinal tract tissue, which may decrease adequacy of the specimen and diagnostic yield. But reinsertion of stylet during each pass increases the procedure time and patient discomfort as stylet needs to be withdrawn after puncturing the lesion and then carefully reinserted through the needle before each pass. Moreover, there may be increased the risk of needle stick injuries to the assistant handling the needle, and sometime it is difficult to remove the stylet after lesion has been punctured.

Table 1: Baseline characteristics of S^+ and S^- groups

Characteristic	S^+ (n=66)	S^- (n=62)	P
Mean age±SD	51.9±12.5	56.8±16.8	0.06
Gender (males, %)	40 (60.6)	41 (66)	0.58
Site of lesion (n, %)			
Pancreas	23 (34.8)	20 (32.2)	0.90
Mediastinal lymph node	20 (30.3)	19 (30.6)	0.88
Abdominal lymph node	13 (19.6)	15 (24.1)	0.69
Liver	5 (7.5)	3 (4.8)	0.78
GIT subepithelial lesion	2 (3.0)	2 (3.2)	0.66
Others	3 (4.5)	3 (4.8)	0.73
Size of lesion (mean±SD)	24.6±14.2	22.8±15.1	0.48

SD=Standard deviation, GIT=Gastrointestinal tract

Table 2: Comparison of adequacy of specimen, amount of blood on slide, number of passes required and diagnostic yield

Characteristic	S^+ (n=66)	S^- (n=62)	P
Sample adequacy (%)			
Adequate	59 (89.4)	55 (88.7)	1.00
Inadequate	7 (10.6)	7 (11.3)	
Amount of blood on slide (%)			
Minimal	34 (51.5)	31 (50)	0.92
Moderate	21 (31.8)	19 (30.6)	
Significant	11 (16.6)	12 (19.3)	
Number of passes (mean±SD)	2.16±0.94	2.34±1.06	0.49
Diagnosis			
Benign	29 (43.9)	26 (41.9)	0.86
Malignant	27 (40.9)	24 (38.7)	
Suspicious of malignancy	3 (4.6)	5 (8.1)	
Inadequate	7 (10.6)	7 (11.3)	

SD=Standard deviation

Table 3: Sample adequacy and number of passes for lymph node and pancreatic lesions

	S^+	S^-	P
Lymph node, n	33	34	
Adequate sample, n (%)	30 (90.9)	31 (91.1)	1.0
Number of passes (mean±SD)	1.9±0.82	2.0±0.91	0.63
Diagnosis, n (%)			
Benign	17 (51.5)	18 (52.9)	0.75
Malignant	12 (36.4)	10 (29.4)	
Suspicious of malignancy	1 (3.0)	3 (8.8)	
Inadequate	3 (9.1)	3 (8.8)	
Pancreas, n	23	20	
Adequate sample, n (%)	21 (91.3)	17 (85)	0.65
Number of passes (mean±SD)	2.3±1.13	2.41±1.24	0.76
Diagnosis, n (%)			
Benign	7 (30.4)	6 (30.0)	0.97*
Malignant	12 (52.2)	11 (55.0)	
Suspicious of malignancy	1 (4.3)	1 (5.0)	
Inadequate	3 (13.0)	2 (10.0)	

*To make data values valid, suspicious of malignancy and inadequate samples were used as combined. SD=Standard deviation

In this prospective study, 128 lesions with comparable baseline parameters were randomized to undergo EUS-FNA with and without a stylet. There was no statistically significant difference between the two groups with regard

to the adequacy of the specimen, amount of blood on the slide, number of passes and diagnostic yield. Some of the characteristics of the lesions like consistency and path of the needle may be a source of bias when comparing all the lesions combined. So, we separately analyzed lymph node and pancreatic lesions and again, did not find any significant difference. There is limited data comparing the use of EUS-FNA with or without a stylet, and none of the studies has shown any advantage of using a stylet. Most of the studies in the literature have been retrospective. In a retrospective analysis, Wani *et al*. compared EUS-FNA with and without a stylet in 228 lesions. The authors did not find a significant difference in adequacy of the specimen, cellularity, contamination and diagnostic accuracy.[11] Devicente *et al*., in their retrospective analysis of 54 lesions, also found similar results.[10] In a prospective analysis, Sahai *et al*., studied 46 lesions divided equally into with stylet and without stylet group, and they did not find any significant difference in the diagnostic accuracy.[12] They also found that sample adequacy was lower and bloodiness higher in the with stylet group, which suggest that quality of samples with stylet may actually be inferior. Another prospective randomized controlled trial failed to show any benefit of the use of stylet.[14]

All these studies have been from the west, and there is no study from the Indian subcontinent where pattern of diseases is different. Infectious diseases including tuberculosis are more common in the developing countries. In our study also, benign etiology of lymph node lesions was more common, which supports the higher prevalence of infections.

There were certain limitations of our study. Though this study was conducted at a high volume center, the duration of data compilation was <1 year and as a result the sample size was relatively small. A study with a larger sample size is needed to conclusively refute the need for a stylet during EUS-FNA. The cytopathologist had not commented on the contamination of slides with normal gastrointestinal wall tissue with has been considered to be the major advantage of a stylet in the needle. But this limitation is not of much importance if the cytopathologist finds the samples adequate to make a conclusive diagnosis of a benign or malignant disease.

To have uniformity in the groups only 22-gauge EUS-FNA needle was used, which may limit the generalized applicability for other sizes of needles. Suction was used in all the samples, which may have affected the amount of blood on slides. We did not use the same lesion to compare the two groups. One of the reasons for this approach was, only a single pass was made in some lesions when sample was considered to be adequate. Another reason was to avoid bias due to sequence of passes, where subsequent passes may have more contamination with blood. So we compared the separate lesions, which may limit the strength of our study. Majority of the samples were from lymph nodes and pancreas, which leaves a lacuna regarding applicability for other lesions. Because of this limitation, we have also separately analyzed and compared these two groups. The diagnosis was made solely on the basis of cytology results, which needs to be confirmed with histopathology examination. Moreover, follow-up data of patients treated on the basis of cytology results were not analyzed, which may be a source of bias.

In conclusion, this prospective randomized controlled single-blind study shows that use of a stylet during EUS-FNA does not confer any advantage regarding sample adequacy, bloodiness of sample, number of passes and diagnostic yield for benign or malignant disease. If some more studies from the various other regions of the world also show similar results, abandoning the use of a stylet during EUS-FNA may be considered.

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How to cite this article: Nijhawan S, Singh B, Kumar A, Ramrakhiani D, Mathur A, Gupta G. Randomized controlled trial of comparison of the adequacy, and diagnostic yield of endoscopic ultrasound guided fine needle aspiration with and without a stylet in Indian patients: A prospective single blind study. J Dig Endosc 2014;5:149-53.

Source of Support: Nil, **Conflict of Interest:** None declared.