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Research Paper

Transoral flexible laryngoscope biopsy: Safety and accuracy

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Abstract *Objective:* To determine the accuracy of transoral flexible laryngoscope (TFL) biopsy and also to identify the safety as office based procedure in terms of complications.
Methods: This is a diagnostic study; the type of intervention is outpatient department based biopsy of laryngeal lesions. All patients seen in ENT outpatient department of Lyari General Hospital with suspicious lesions of Larynx were referred for Transoral Flexible Laryngoscopy Biopsy under local anesthesia. The specimens were sent for histopathology. The patients with benign pathology or carcinoma in situ were referred for direct laryngoscopy and biopsy. The sensitivity and specificity were calculated and the frequencies of complications were monitored to determine the complication rate.
Results: During the course of study a total of 47 patients underwent TFL biopsy in office settings. Out of these patients 16 patients were referred for direct laryngoscopy biopsy. The study population included 32 men and 15 women with ages ranging from 28 to 52 years and mean of (39 ± 6) years. Among 43 patients squamous cell carcinoma was the final diagnosis in 31 patients. In the rest of 12 patients' dysplasia and benign lesion was the diagnosis in 9 and 3 patients respectively. These 12 patients underwent direct laryngoscopy biopsy and 10 of them diagnosed with invasive carcinoma rest had benign lesions. Hence the specificity was 75.6% and sensitivity was 100%. None of the patients developed any serious complication.

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Conclusions: All patients with a suspicious lesion diagnosed by TFL biopsy as being benign or carcinoma in situ should have direct laryngoscopy for verification of the findings. But the results positive for carcinoma are reliable. In addition, this is a safe procedure.

Introduction

Transoral flexible endoscopes has been used since many decades for obtaining histopathological specimens from upper gastro-oesophageal system,[1] but its application in laryngeal and hypopharyngeal lesions is not old. In 1970 transoral flexible laryngoscope (TFL) was used for this purpose for the first time.[2] Since its evolution, the advancement in the magnification and illumination techniques have made it possible for the otolaryngologist to use the flexible laryngoscope for various procedures,[3,4] in addition to that due to improvement in local anesthesia techniques many of these procedure can be done safely in office settings as well. Direct laryngoscopy and biopsy has traditionally been the gold standard for the diagnosis of laryngeal and hypopharyngeal lesions but the advent of flexible scopes with biopsy channel has theoretically replaced it. The international literature has consistently shown that TFL biopsy is a safe method, however its accuracy is still debatable. This is the primary aim of this study to determine the accuracy of TFL biopsy and also to identify its safety as office based procedure in terms of complications.

Method

This is a diagnostic study. All patients seen in otolaryngology clinic of Lyari General Hospital with suspicious lesion of larynx and hypopharynx underwent office based biopsy of the lesions under local anesthesia. An ulceration or whitish leukoplakic patch of mucosa is considered as a suspicious lesion if it remained there for more than two weeks. All biopsies that were performed from December 1, 2013 to August 31, 2015 were included in study after taking written informed consent, those who refused were excluded. The biopsy specimen were obtained through TFL and sent for histopathological examination to confirm either a benign or malignant lesion.

The patients with diagnosis of dysplasia or benign pathology were offered direct laryngoscopy and biopsy however the patients in which diagnosis of invasive carcinoma was made by TFL were offered treatment accordingly. The demographic and clinical data was recorded, sensitivity and specificity were calculated and the frequencies of complications were also monitored to determine the complication rate.

Procedure details

We used 6 mm flexible laryngo-bronchoscope with 2.8 mm biopsy and suction channel to obtain the specimen from suspicious lesions. This is an Olympus made scope, BF type TE2, which is attached to HD camera monitor system of Stryker and xenon light source. The lignocaine 4% gargle were used to obtain adequate anesthesia, 5 ml of lignocaine 4% nebulization and was also used in patients having pathology limited to vocal folds only. The flexible scope was passed through a mouth piece placed in oral cavity, 2.8 mm cup forceps was then passed through the biopsy channel and biopsy was obtained. In almost all instances more than one specimen was taken and preserved in plastic bottles containing 10% formalin. The patients were observed for 30 min for any complications and were sent home with advice to follow after 10 days. If they had any signs of complication were offered overnight admission.

Results

During the course of study a total of 47 patients underwent TFL biopsy in office settings. Out of these patients 16 patients were referred for direct laryngosocpy biopsy afterwards but 4 of them refused for the procedure hence were excluded, finally 43 patients were included. The study population included 32 men and 15 women with ages ranging from 28 to 52 years with mean of (39 $\pm$ 6) years. The hoarseness of voice and dysphagia were the two most common symptoms seen in 26 and 17 patients comprising of 60.5% and 39.5% respectively. Twenty-one patients nearly half of the study population (48.8%) did not have any comorbid, the different comorbid states were shown in Table 1.

Glottic lesions were the most frequent occurrence seen in 16 (37.2%) patients, the post cricoid lesion was identified in only 5 patients whereas supraglattic and pyriform fossa lesion were seen in 11 patients each.

In all patients adequate specimen was obtained. Among 43 patients squamous cell carcinoma was the final diagnosis in 31 patients. In the rest of cases dysplasia and benign lesion were the diagnosis in 9 and 3 patients respectively. Those 12 patients underwent direct laryngoscopy biopsy and 10 of them diagnosed with invasive carcinoma whereas 2 had benign lesions.

That determined the accuracy of TFL biopsy shown in Table 2. Specificity was 75.6%, sensitivity was 100%.

Table 1 Comorbid number and frequency.

Comorbid	Number of patients	Frequency (%)
Hypertension	12	27.9
Multiple	10	23.3
None	21	48.8

Table 2 The accuracy of TFL biopsy.

Parameters	Cases
True positive	31
False negative	10
False positive	0
True negative	2

Only one patient developed post procedure blood tinged salivation and chocking sensation, that patient was admitted for overnight observation and treated conservatively.

Discussion

Since its dawn in Brazil in 1807 the endoscopy has gone through several revolutions.[5] In 90's once introduced in ENT, was used only for the purpose of visualization of laryngeal structures. Later on endolaryngeal procedures were started in operating room to replace open laryngeal surgeries. However today, office-based procedures by means of new technologies, such as flexible laryngoscopy, are becoming popular, mainly because it provides the utility of avoiding general anesthesia and a tour to operating room and offering a simple and cost-effective alternative to the traditional direct laryngoscopy procedures in a less invasive fashion, especially for patients who are not candidates for general anesthesia or laryngeal suspension.

The biggest dilemma is the accuracy of TFL biopsy in comparison to direct laryngoscopy biopsy. According to our study, the specificity of TFL in diagnosing invasive carcinoma is comparable, but the sensitivity of diagnosing a suspicious lesion is low. These results may point to the fact that direct laryngoscopy represents the gold standard diagnostic procedure whenever the specimen obtained in an in-office TFL procedure is interpreted as a non-malignant lesion. This conclusion reflects the findings of several recent studies, although the comparison is not direct. Cohen et al[6] concluded 96% specificity and 69% sensitivity of TFL biopsy in 91 office based procedures. The higher accuracy achieved in our study presumed due to small sample size. Similarly 100% accuracy of trans nasal esophagoscopy in 17 patients with lesions of the upper aero digestive tract was reported by Postma et al.[7] The diagnosis was then confirmed later by pan endoscopy and biopsy. The results of trans nasal esophagoscopy and pan endoscopy with biopsy specimens were similar. This seems to be due to absence of gag and cough reflex which makes it easier to obtain multiple specimens from esophagus hence can attain higher accuracy. Price et al[8] reviewed the findings on 18 patients who underwent trans nasal flexible laryngo-esophagoscopy either for localization of a primary cancer or investigation of the upper aero digestive tract (12 cases of laryngeal lesions). Those authors uttered apprehension that the size of the acquired biopsy specimen might result in underestimation of the depth of invasion. However trans nasal flexible laryngo-esophagoscopy was not compared with gold standard direct laryngoscopy in cases with results indicating benign lesions. Wang et al[9] evaluated the efficacy of trans nasal esophagogastroduodenoscopy performed without sedation in the diagnosis of esophageal lesions and reported an 11.1% rate of inaccurate diagnosis among 27 patients with hypopharyngeal cancer. The conclusions of these studies were obtained from results derived from smaller data than the one reported herein and were not compared with other studies: this may explain the higher accuracy described in older reports.[7–9]

It has been observed that pathologists are reluctant in concluding malignancy from small biopsy specimens. It's being supported by Sarioglu et al[10] when laryngeal preneoplastic lesions were evaluated by 14 pathologists using the World Health Organization, Ljubljana and squamous intraepithelial neoplasia classification systems.[10–17] All 42 laryngeal biopsy specimens were labeled as squamous hyperplasia; mild, moderate, or severe dysplasia; carcinoma in situ; or invasive carcinoma. Sarioglu et al concluded that there exists a difference of opinion between the participants in all 3 classification systems, and they questioned intra-observer accuracy. The lack of willingness on the part of pathologists to commit to a final diagnosis of carcinoma in situ/invasive carcinoma on the basis of small fragments of tissue obtained via TFL is also seen in our 9 patients who initially labeled as dysplasia and later on confirmed as invasive carcinoma on direct laryngoscopy biopsy.

An inherent error in laryngeal biopsies on final pathologic evaluation is the diagnosis of dysplasia on the basis of the basement membrane appearing intact microscopically. This diagnosis, often may overlook other parts of the vocal fold that otherwise may contain invasive carcinoma. This might partially explain the low sensitivity in the TFL group when small and unrepresentative material is initially diagnosed as dysplasia and later diagnosed as invasive carcinoma on direct laryngoscopy biopsies.

Lippert et al[18] have reported the complication rate of less than 1% has concluded that TFL biopsy is a safe procedure to be undertaken in office settings. In our cohort of patients only one developed mild blood tinged salivation which was resolved by conservative means and the patient remained stable without any airway compromise thus ensuring the safety of patient in this procedure and afterwards.

We used fiber optic equipment to obtain the laryngeal view in our study. Perhaps with improved visualization equipment that use newer distal chip endoscopes and different lighting algorithms (eg, narrow-band imaging), we would be able to improve the diagnostic accuracy.

In conclusion, the lower specificity for diagnosing suspicious lesions of the larynx using TFL with biopsy raises serious concerns about its clinical impact. As such, it is recommended that all patients with a suspicious lesion diagnosed by TFL biopsy as benign or carcinoma in situ should have direct laryngoscopy for verification of the findings. But the results positive for carcinoma are reliable. In addition this is a safe procedure can be offered in office settings without fear of airway compromise.

Declaration of interest

All authors have disclosed that there exists no conflict of interest either financial or personal relationships with other people or organizations that could inappropriately influence (bias) this work.

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