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Original Article

Contact Endoscopy of mucosal lesions of oral cavity – Preliminary experience

Col Awadhesh Kumar Mishra^{a,*}, Col Ajith Nilakantan^b, Col Kavita Sahai^c,
Col Rakesh Datta^d, Col Ajay Malik^c

^a Senior Advisor (ENT), Military Hospital, Jalandhar Cantt, India

^b Senior Advisor (ENT), Army Hospital (R&R), Delhi Cantt, India

^c Senior Advisor (Pathology & Oncopath), Base Hospital, Delhi Cantt, India

^d Senior Advisor (ENT), Base Hospital, Delhi Cantt, India

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ABSTRACT

Background: Contact Endoscopy is a non invasive tool to visualise alterations in cell architecture in vivo. In this study we investigated the diagnostic accuracy of Contact Endoscopy in detecting malignancy in oral mucosal lesions.

Methods: 76 patients with oral mucosal lesions requiring biopsy were included. Contact Endoscopy was performed by Otolaryngologist before biopsy and findings recorded. The lesion was then biopsied and sent for histopathological examination by Pathologist who was blinded to Contact Endoscopy findings. Findings of Contact Endoscopy were compared with histopathological findings taking the latter as the gold standard. Two biopsies were reported as 'inconclusive' on histopathological examination and hence excluded from the final analysis. Data of the remaining 74 patients is presented here.

Results: Clinically lesions were diagnosed as ulcero-proliferative lesions in 34 patients, Leukoplakia in 19, Erythroplakia in 9, Lichen planus in 5 and Submucous fibrosis in 7 patients. Histopathological examination revealed presence of malignancy in 97.06% of ulcero-proliferative mucosal lesions, 10.53% of leukoplakia and 33.33% of erythroplakia while corresponding figures on Contact Endoscopy were 94.12%, 5.26% and 11.11% respectively. No malignancy was detected in lichen planus and submucous fibrosis by either technique. When compared with histopathological examination, CE showed sensitivity of 84.21%, specificity of 94.44% and accuracy of 89.19%. No adverse effects on the patients were seen due to the procedure or stain.

Conclusion: Contact Endoscopy may be useful in determining cellular structure in vivo without biopsy to detect oral malignancy early. Further studies are suggested.

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* Corresponding author. Tel.: +91 9876026564 (mobile), +91 9560111766.

E-mail address: buddhiprakash@rediffmail.com (A.K. Mishra).

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Introduction

Oral carcinoma is a major health problem in India as it is the commonest cancer among males and the third commonest among females in India. In fact, India accounts for 86% of the total oral cancer figure across the globe according to National Institute of Health and Family Welfare (NIHFW). It has also been shown that successful treatment of this condition depends on the T stage of the tumour at presentation. It is therefore of paramount importance to diagnose this condition early.

Almost 90% of oral tumours are squamous cell carcinoma (SCC) and arise from the oral mucosal lining.¹ Apart from frank ulcero-proliferative growths in oral cavity, we also encounter many other mucosal lesions like leukoplakia, erythroplakia etc which may harbour malignancy. To detect the presence of malignancy in these lesions surgical biopsy for histopathological examination (HPE) is the gold standard. However, this procedure is invasive and has many other disadvantages like delay in getting the report, local scarring, bleeding and difficulty in interpretation in post radiation cases. This has led to the quest for a non invasive technique capable of showing histopathological picture in vivo. Consequently, many non invasive techniques have been tried like 5-aminolevulinic acid induced protoporphyrin IX fluorescence,² autofluorescence using helium cadmium laser,³ Indirect fluorescence,⁴ Spectrometric measurement,⁵ Narrow Band Imaging,⁶ Optical Coherence Tomography^{7,8} etc. A detailed review of such techniques has been given by Hughes et al.⁹

Contact Endoscopy (CE) is one of these techniques which additionally has a unique capability of demonstrating actual cellular architecture in vivo and provide instantaneous diagnosis. This technique was described by Hamou in 1979 for visualization of cervical and uterine epithelial cells for screening and diagnosis of cervical and uterine pathology.¹⁰ Andrea et al used CE as a diagnostic tool in the evaluation of various pathologies in the larynx in 1995.^{11,12} Since then CE has been used for in vivo diagnosis of lesions of many sites in head and neck as well as other regions.^{13–20}

Even though limited research does show a benefit of using CE in diagnosis of dysplastic lesions in the oral cavity, there is a need for more studies. This is especially important in the Indian context where oral squamous carcinoma is widely prevalent and no previous study using CE has been reported.

Material and methods

The study was carried out in a tertiary level hospital on consecutive patients presenting to the hospital with a mucosal lesion in the oral cavity requiring surgical biopsy as per the current medical practice and guidelines from Jan 2012 to July 2013. Any lesion not meriting surgical biopsy as per current medical practice was excluded. Informed consent for CE as well as surgical biopsy was taken. CE was employed to study the lesion first followed by surgical biopsy in the same sitting.

The technique of CE

CE was performed by one of the Otolaryngologists. No anaesthesia was required. After sucking out the secretions and wiping off saliva, a zero degree contact endoscope (model: Andrea-Dias Contact Micro Laryngoscope with HOPKINS Straight Forward Telescope 0°, diameter 5.5 mm, length 23 cm manufactured by Karl Storz) (Fig. 1) was gently placed over the mucosa and moved slowly over the area of interest. The procedure was performed at 60× and 150× magnifications. Images were digitally captured by the camera and were stored both as photograph and video. Vascular patterns were studied without staining as the stain prevents penetration of light into submucosal plane where the blood vessels lie. Thereafter, the lesion was stained by placing cottonoids soaked in 1% Methylene blue against it for five minutes (or more if the staining was inadequate). The stained area was then studied by repeating the procedure mentioned above. Cellular architecture was now seen clearly – nuclei appearing as dark blue structures while cytoplasm was light blue. The images were

Fig. 1 – Zero degree contact micro laryngoscope (Karl Storz).

then analysed by the Otolaryngologist and findings as well as interpretation was recorded. The interpretation of CE images was based on features of various lesions already described by previous workers for oral cavity and other areas of upper aero–digestive tract.^{11–13,21–24}

These features include homogeneousness of distribution of cells, number of cells per field, uniformity of nucleus staining, hyperchromatism, nuclear – cytoplasmic ratio, nuclear and cellular pleomorphism, prominent nucleoli, presence of mitotic figures etc. Additionally, the pattern of distribution, branching and coiling of blood vessels as well as rate of flow of RBCs inside the blood vessels seen on CE of unstained lesion was also taken into account.

The technique of HPE

After performing CE, the stain was washed away and 2% lignocaine with 1 in 1 lac adrenaline was infiltrated locally for local anaesthesia. Surgical biopsy was then performed (punch/incision/excision biopsy as dictated by clinical settings). Specimen was sent to the pathologist who was blinded to CE findings. An Otolaryngologist in the team who had not performed CE or interpreted the CE findings, compared the CE diagnosis given by otolaryngologist against the HPE report given by the pathologist. Patients underwent definitive treatment as per the HPE report and in accordance with current medical practice.

Results

There were 76 patients enrolled during the period of study. However, HPE report in 02 of them was inconclusive due to

technical reasons and therefore excluded from the study. Thus, the data presented here includes only 74 patients – 45 males and 29 females, having ages from 21 years to 73 years. Average age was 56.35 years. Clinical lesions comprised ulcero-proliferative lesion in 34 patients, Leukoplakia in 19, Erythroplakia in 9, Lichen planus in 5 and Submucous fibrosis in 7 patients. Representative images obtained on CE and HPE are shown in Figs. 2–5.

The HPE reports revealed presence of malignancy in 97.06% of ulcero-proliferative mucosal lesions, 10.53% of leukoplakia and 33.33% of erythroplakia while corresponding figures on CE were 94.12%, 5.26% and 11.11% respectively. No malignancy was detected in lichen planus and submucous fibrosis by either technique (Table 1).

When compared with the HPE diagnosis, CE showed a sensitivity of 84.21%, specificity of 94.44% and accuracy of 89.19%. Predictive value of positive test (PPV) was 94.11% while predictive value of negative test (NPV) was 85% (Table 2).

CE could be performed in the OPD itself and with ease in most cases. It was well tolerated by the patients. Difficulties were faced in some patients in keeping the endoscope steady and on account of bleeding on touching friable growths, artefacts due to precipitation of stain in the tissues, interference by saliva, washing away of stain by saliva/secretions before completion of procedure (forcing re-staining) etc. No adverse effects on the patients were seen due to the procedure or stain.

Discussion

For favourable outcome of treatment of oral malignancies, early diagnosis is of utmost importance. Towards this aim, it

Fig. 2 – Vascular patterns seen on CE of unstained lesions. (150×) A: Normal blood vessels in cheek. Minimal branching. No coiling or micro haemorrhages. Lay out is parallel. Flow of RBCs inside the vessels was brisk. B: Numerous tufts of vessels seen in lichen planus. C: Numerous dilated blood vessels in erythroplakia D: Blood vessels in malignant lesion showed coiling, micro haemorrhages and increased tortuosity of vessels. Flow of RBCs inside the vessels was sluggish.

Fig. 3 – A: CE image of normal cheek (150×). Note the uniform pattern of cells and nuclei. Nuclear – cytoplasmic ratio also uniform and less than one. No mitotic figure. B: Corresponding HPE image. (H&E stain, 200×). Reactive changes with mild keratinisation is seen. C: CE image of leukoplakia of cheek (150×). Cells are more or less uniform with normal nuclear – cytoplasmic ratio. Acellular areas of keratin deposition present. D: Corresponding HPE image (H&E stain, 200×). Reactive changes with acanthosis, keratinisation and inflammation in submucosa seen.

Fig. 4 – A: CE image of lichen planus (150×). Slight variation in size and shape of cells and nuclei is seen. There is infiltration by inflammatory cells. B: Corresponding HPE image (H&E stain, 200×). Intense infiltration by inflammatory cells is evident. C: CE image showing Dysplasia (150×). Cell distribution is not homogenous. Nuclei slightly larger. Some amount of variation in size and shape of cells as well as nuclei can be noticed. D: Corresponding HPE image (H&E stain, 400×). Full thickness dysplasia is evident. There is intense inflammation, oedema and capillary proliferation in submucosa. Separation of submucosa from mucous membrane seen in the image is an artefact due to processing of tissue.

Fig. 5 – A: CE image of floor of malignant ulcer (150×). Field contains mostly necrotic material which failed to take up the stain. Only few cells are seen with poor staining. Nuclei are large and spongy with irregular staining (heterochromatic). Pyknotic nuclei (blue arrow), prominent nucleoli (white arrows) and probably mitotic figures (black arrow) are present. B: Corresponding HPE image (H&E stain, 200×). Hyper chromatic nuclei with extensive cellular as well as nuclear pleomorphism are seen.

is essential to closely monitor all mucosal lesions especially premalignant lesions. The risk of malignant transformation in leukoplakia has been reported as 3.6–20%, and slightly higher in erythroplakia.^{25,26} Lichen planus and Submucous fibrosis also may have a risk of malignant transformation.²⁷ In our study, 10.53% of Leukoplakia and 33.33% of Erythroplakia had evidence of malignancy on HPE. No malignancy was detected in lichen planus and submucous fibrosis. However, no conclusion can be drawn due to small number of Lichen planus and Submucous fibrosis in our study.

Surgical biopsy due to its inherent morbidity and difficulties cannot be employed for this purpose freely and due thought is to be given before taking biopsy. A non invasive, repeatable and reliable technique is therefore the need of the hour. In our study, CE passed on all these accounts. The

sensitivity, specificity and accuracy of CE in our study were very high and in line with the results of other workers.^{14,21,22,28}

Sensitivity of CE was comparatively on lower side. It occurred on account of not being able to detect few cases of Carcinoma in situ (Ca in situ) and very early invasive carcinoma. Both these conditions originate at the level of basement membrane first and are not picked up by CE due to poor penetration of stain and light into deeper layers of epithelium. Thus, some delay in diagnosis can occur till abnormal cells migrate to upper layers. We also could not classify dysplasia into mild, moderate and severe categories on CE. This classification is given on HPE by seeing the changes across the thickness of mucous membrane from deep to superficial, while in CE view is 'end on' and hence all layers get superimposed on each other. Therefore, one has to rely on nuclear

Table 1 – Summary of HPE & CE diagnosis of clinical lesions.

Clinical diagnosis HPE/ CE Diagnosis	↔	Ultero-proliferative lesion	Leukoplakia	Erythroplakia	Lichen planus	Submucous fibrosis	Total
	↕	(34)	(19)	(9)	(5)	(7)	(74)
HPE diagnosis (n = 74)							
Verrucous carcinoma		1	0	0	0	0	1
Well differentiated SCC		13	1	1	0	0	15
Moderately differentiated SCC		12	0	0	0	0	12
Poorly differentiated SCC		7	0	0	0	0	7
Ca in situ		0	1	2	0	0	3
Severe dysplasia		1	5	3	0	1	10
Moderate dysplasia		0	3	1	0	0	4
Mild dysplasia		0	2	0	0	0	2
No dysplasia		0	7	2	0	0	9
Lichen planus – no malignancy		0	0	0	5	0	5
Submucous fibrosis – no malignancy		0	0	0	0	6	6
CE diagnosis (n = 74)							
Malignant lesion		32	1	1	0	0	34
Dysplasia		2	11	6	0	0	19
Benign lesion		0	7	2	3	2	14
Lichen planus – no malignancy		0	0	0	2	0	2
Submucous fibrosis – no malignancy		0	0	0	0	5	5

SCC = Squamous Cell Carcinoma, Ca in situ = Carcinoma in situ.

Table 2 – CE as a predictor of malignancy in oral mucosal lesions (n = 74).

Lesion found malignant on CE (test procedure)	Lesion found malignant on HPE (Gold Standard)	
	Yes	No
Yes	32 (TP)	2 (FP)
No	6 (FN)	34 (TN)

TP = True Positive, FP= False Positive, TN = True Negative, FN = False Negative, Sensitivity = 84.21%, Specificity = 94.44%, Accuracy = 89.19%.
Predictive value of positive test = 94.11%, Predictive value of negative test = 85%.

and cellular structural changes only for diagnosis. Lower sensitivity of CE in our study can also be attributed to need of training and learning curve to some extent. More experienced researchers have reported sensitivity of even 100%.²¹

On the positive side, CE allowed 'in vivo' examination of cellular architecture and vascular pattern of the mucosa and could be repeated as many times as needed. Unlike a small area studied by HPE, it could scan large areas quickly. This feature can be of great help in selection of most suitable area for biopsy. It avoids damage and alterations in tissues which can occur due to biopsy or due to processing of tissue for histopathological examination. The video and images could be saved and reviewed as desired.

At present we do not recommended CE to substitute biopsy and HPE. Perhaps, it may have utility in deciding the most suitable area for taking biopsy and serial follow up of precancerous lesions.

Based on the findings of present study we regard CE as a promising non invasive technique to know cellular architecture and vascular patterns in vivo for evaluation of oral mucosal lesions due to its simplicity and high sensitivity, specificity and accuracy. However, further studies and research to improve the technique are required.

Conflicts of interest

All authors have none to declare.

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