Review

The assessment of accuracy of cytobrush technique and spatula technique when compared to the histopathology in the diagnosis of oral premalignant and malignant lesions

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Abstract
This comparative study was conducted to analyze the cytological smears prepared from oral premalignant and malignant lesions by the use of two cytological techniques.
The smears taken with spatula from oral premalignant lesions showed epithelial cells predominantly from superficial and intermediate cell layers. A few parabasal cells were also seen in smears taken from ulcerative leukoplakia lesions. But smears taken with the cytobrush showed cells from all three layers of the epithelium with a good cell harvest.
In analysis, we found a statistically significant difference between the two cytological techniques used for the diagnosis of squamous cell carcinoma and dysplasia. The the cytobrush technique appeared to be as accurate as the histopathological technique.

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Introduction

Oral cancer is a serious disease in which many cases have a disastrous outcome. Annually 20,000 new cancer patients are detected in Sri Lanka, from which 1500-2000 cases are oral cancers. It is the highest-ranking malignant tumor in Sri Lanka. Deaths form oral cancer in Sri Lanka is 1095 per year. Therefore, it is a major health problem in Sri Lanka (1).

Population screening is an accepted method of reducing the morbidity & mortality. But clinically differentiating the premalignant and malignant lesions from similar looking benign lesions at an early stage is difficult (2). As scalpel biopsy is invasive & associated with potential morbidity, many oral lesions are subjected to biopsy only when they display the features of malignancy, while innocuous looking early stage cancerous lesions are merely observed clinically. This may be the reason, in part, for more than 50% of oral cancers to be diagnosed in the advanced stage. Therefore, early detection of apparently innocuous oral cancers is mandatory. The above situation leads to the necessity of a simple technique to diagnose oral cancer in its early stages and to predict the behavior of epithelial dysplasia.

Since 1992, a number of cytological studies has been conducted using the cytobrush technique for the above purpose, but all these studies concentrated on the test diagnostic characteristics like sensitivity and specificity. Even the largest study conducted in 1999 (3) is incomplete as the cytological diagnosis of 618 smears were not compared with their histopathological diagnoses. Therefore, it is necessary to do further studies before using the cytobrush as a diagnostic instrument (screening technique) by comparing the diagnosis made by the cytobrush technique with the histopathological technique in the diagnosis of malignant and premalignant lesions.

Almost all the above studies using cytobrush technique were conducted in western countries where the majority of leukoplakia lesions are due to smoking (4) and not due to chewing betel as in India and Sri Lanka (5). Normally, the keratotic layer of leukoplakia lesions due to chewing betel is thicker than that due to smoking tobacco. Therefore, it was decided to find out whether the same cytobrush technique will be equally effective in diagnosing the leukoplakia lesions in the Sri Lankan population.

Methodology

Subjects were selected according to their clinical presentation as oral premalignant lesions and oral carcinoma from Oral and Maxillo-facial units of Teaching Hospitals, Galle, Kandy, Peradeniya and

General Hospital, Matara. Prior to the study informed written consent was taken from the subjects.

Two cytological smears were taken from the same lesion by using a cytobrush plus cell collector and a metal spatula by complete randomization procedure. Subsequently a surgical biopsy was taken from the same lesion for the tissue diagnosis.

Cytological smears were stained with modified papanicolaou staining technique and histological sections with H & E. The cytological smears were assessed using a light microscope. In assessment of a cytological smear, the whole cytological smear was examined and the gradings were performed under high power (x40). According to the findings diagnosis was made as Normal, Inflammation, Keratosis / Hyperkeratosis, Dyskaryosis (mild, moderate, severe), Carcinoma and Inadequate smear.

Methods of statistical analysis

We evaluated these different techniques by calculating sensitivity, specificity, accuracy, positive and negative predictive values and also used Chi-squared goodness of fit test to test whether an observed frequency distribution of diagnoses by two cytological techniques deferred significantly from the histopathological diagnosis.

Results

Cytological diagnosis of clinically malignant lesions

Final results of the histological and cytological analysis are show an in the Table 1. In statistical analysis, 4 non-squamous cell carcinoma lesions and 3 inadequate cytological smears were removed. Therefore the number of clinically malignant lesions studied was 69.

1. **Comparison of spatula and cytobrush techniques with the biopsy technique in the diagnosis of clinically malignant lesions (**Diagnosed as Severe, Moderate, Mild epithelial dysplasia, Squamous cell carcinoma and others**)** A statistically significant difference was observed in between the spatula technique (**X^2 = 23.685; d.f. = 4; p = 0.000)** and the biopsy technique in the diagnosis of oral carcinoma lesions. There was no statistically significant difference between the cytobrush technique (**X^2 = 2.307; d.f. = 4; p = 0.680)** and the biopsy technique.

2. **Comparison of spatula and cytobrush techniques with the biopsy technique in the diagnosis of clinically malignant lesions (**Diagnosed as precancer, cancer and others**)** A statistically significant difference was observed between the spatula technique **(X^2 = 22.306; d.f. = 2; p = 0.000)** and the biopsy technique in the diagnosis of clinically malignant lesions. There was no statistically significant difference between the cytobrush technique (**X^2 =1.910; d.f. = 2; p = 0.385)** and the biopsy technique.

3. **Comparison of spatula technique with cytobrush technique in the diagnosis of clinically malignant lesions (**Diagnosed as Severe, Moderate, Mild epithelial dysplasia, Squamous cell carcinoma and others**)** A statistically significant difference was observed between the use of spatula technique (**X^2 = 11.397; d.f. = 4; p = 0.022)** and the cytobrush techniques in the diagnosis of clinically malignant lesions.

4. **Comparison of spatula technique with the cytobrush technique in the diagnosis of clinically malignant lesions (**Diagnosed as pecancer, cancer and others**)** A statistically significant difference was observed between the use of spatula (**X^2 = 10.524; d.f. = 2; p = 0.005)** and the cytobrush techniques in the diagnosis of clinically malignant lesions.

Therefore, in the diagnosis of oral cancer and precancerous lesions, the cytobrush technique is as effective as the biopsy technique. The cytobrush technique is also more effective than the spatula technique in the diagnosis oral malignant and premalignant lesions.

Evaluation of diagnosis of clinically malignant lesions

To evaluate the cytological diagnosis of oral squamous cell carcinoma by the spatula and the cytobrush techniques, the sensitivity, specificity and the accuracy rates were calculated. Thereafter the chi-squared test was applied to find out whether the observed differences of these figures were due to chance alone or not.

Spatula technique

(a) Evaluation of diagnosis of precancers in clinically malignant lesions

Sensitivity = 88.89%, Specificity = 64.71%, Accuracy = 71.01%, PPV = 47.06%, NPV = 94.29%

(b) Evaluation of diagnosis of cancers in clinically malignant lesions

Sensitivity = 60.42%, Specificity = 95.24%, Accuracy = 71.01%, PPV =96.67% NPV = 51.28%

Table 1 Histopathological and cytological diagnosis of clinically malignant lesions

Histopathological Diagnosis	No. of cases	Cytological Diagnosis	Spatula	Cytobrush
Chronic Abscess	01	Inflammation	01	01
Mucus Cyst	01	Normal	01	01
Keratosis	01	Keratosis	01	01
Non-Squamous cell carcinoma	04	Dyskaryosis	04	04
Severe Epithelial Dysplasia	07	Severe Dyskaryosis	03	07
		Moderate Dyskaryosis	02	00
		Mild Dyskaryosis	01	00
		Squamous cell carcinoma	01	00
Moderate Epithelial Dysplasia	09	Moderate Dyskaryosis	07	08
		Mild Dyskaryosis	02	00
		Inadequate Smear	00	01
Mild Epithelial Dysplasia	03	Mild Dyskaryosis	02	03
		Normal	01	00
Squamous cell carcinoma	50	Severe Dyskaryosis	10	03
		Moderate Dyskaryosis	08	02
		Squamous cell carcinoma	29	44
		Keratosis	01	00
		Inadequate Smear	02	01
Total	76		76	76

Table 2 Histopathological and cytological diagnosis of leukoplakia lesions

Histopathological Diagnosis	No. of cases	Cytological Diagnosis Diagnosis	Spatula	Cytobrush
Hyperkeratosis	08	Keratosis	07	07
		Inflammation	01	01
Hyperplasia & Acanthosis	03	Keratosis	03	03
Severe Epithelial Dysplasia	19	Normal	01	00
		Keratosis	01	00
		Severe Dyskaryosis	10	14
		Moderate Dyskaryosis	04	02
		Mild Dyskaryosis	03	02
		Squamous cell carcinoma	00	01
Moderate Epithelial Dysplasia	30	Keratosis	02	01
		Inflammation	01	00
		Moderate Dyskaryosis	15	26
		Mild Dyskaryosis	11	03
		Inadequate smear	01	00
Mild Epithelial Dysplasia	28	Normal	03	00
		Keratosis	01	00
		Inflammation	00	01
		Moderate Dyskaryosis	01	03
		Mild Dyskaryosis	21	24
		Squamous cell carcinoma	01	00
		Inadequate smear	01	00
Squamous cell carcinoma	28	Normal	01	00
		Keratosis	01	00
		Severe Dyskaryosis	01	05
		Moderate Dyskaryosis	05	01
		Mild Dyskaryosis	04	01
		Squamous cell carcinoma	14	21
		Inadequate smear	02	00
Total	116		116	116

Cytobrush technique

(a) Evaluation of diagnosis of precancers in clinically malignant lesions

Sensitivity = 100%, Specificity = 90.20%, Accuracy = 92.75%, PPV = 78.26%**,** NPV = 100%

(b) Evaluation of diagnosis of cancers in clinically malignant lesions

Sensitivity = 89.58%, Specificity = 100%, Accuracy = 92.75%, PPV = 100%, NPV = 80.77%

The above sensitivity, specificity and accuracy figures were compared with the 'gold standard' to find out whether there is any statistically significant difference between them.

1. **Lesions diagnosed as dysplasia by the biopsy technique**
   - **(A) Spatula technique –** Sensitivity was not significant, Specificity was highly significant and accuracy was significant.
   - **(B) Cytobrush technique –** Sensitivity, Specificity and accuracy were not significant.
2. **Lesions diagnosed as carcinoma by the biopsy technique**
   - **(A) Spatula technique** - Sensitivity was highly significant, Specificity was not significant and accuracy was significant.
   - **(B) Cytobrush technique –** Sensitivity, Specificity and accuracy were not significant.

Evaluation of diagnosis of oral leukoplakia

Final results of the histological and cytological analysis are shown in the Table 2.

In statistical analysis, 4 inadequate cytological smears were removed. Therefore, number of leukoplakia lesions studied was 112.

Spatula Technique

(a) Evaluation of diagnosis of precancers (dyskaryosis) in leukoplakia.

Sensitivity = 86.67%, Specificity = 72.97%, Accuracy = 82.14%, PPV = 86.67% , NPV = 72.97%

(b) Evaluation of diagnosis of cancers in leukoplakia.

Sensitivity = 53.85%, Specificity = 98.84%, Accuracy = 88.39%, PPV = 93.33%, NPV = 87.63%

Cytobrush Technique

(a) Evaluation of diagnosis of precancers (dyskaryosis) in leukoplakia.

Sensitivity = 96%, Specificity = 83.78%, Accuracy = 91.96%, PPV = 92.31%, NPV = 91.18%

(b) **Evaluation of diagnosis of cancerous lesions in leukoplakia.**

Sensitivity = 76.92%, Specificity = 98.84%, Accuracy = 93.75%, PPV = 95.24%, NPV = 93.41%

The above sensitivity, specificity and accuracy figures were compared with the "gold standard" to find out whether there was any statistically significant difference between them.

1. **Lesions diagnosed as dysplasia by the surgical biopsy technique**
   - **(A) Spatula technique** - Sensitivity was not significant, Specificity was significant and accuracy was not significant.
   - **(B) Cytobrush technique –** Sensitivity, Specificity and accuracy were not significant.
2. **Lesions diagnosed as carcinoma by the surgical biopsy technique.**
   - **(A) Spatula technique** - Sensitivity was highly significant, Specificity was not significant and accuracy was not significant.
   - **(B) Cytobrush technique** - Sensitivity, Specificity and accuracy were not significant.

Inter-examiner variability

In order to ascertain the diagnostic consistency in the interpretation of cytological smears, forty randomly selected cytological smears were evaluated by the two consultant oral pathologists and by the author himself and they were assessed by the use of chi-squared test. The difference seen in reporting of cytological smears by the three observers were not statistically significant.

DISCUSSION

Even though the oral exfoliative cytology is a simple, painless, economical, rapid and non-invasive procedure, its main disadvantage is the low sensitivity due to inadequate sampling and technical errors (6). The main reason for the inadequate sampling is the inability to get an adequate number of cells from all the cell layers of the epithelium (7). Even though the smears obtained from ulcerated or reddish areas of oral

lesions give an adequate number of cells, in keratotic lesions, the number of cells coming from parabasal and basal layers are few as they are buried beneath the thick mantles of keratinaceous debris.

As this is a comparative study we did not match or controlled the following factors that may have had an effect on the nuclear and cell diameters, i.e. the site of lesion, sex of the patient, presence or absence of anemia or tobacco habits.

Exfoliative cytology of clinically malignant lesions

Use of spatula technique

In the smears prepared by using the spatula technique, the total number of cells present in each smear were less than that of smears prepared by the use of a cytobrush. This finding is similar to the one observed by Ogden et al. in 1992 (8). The majority of cells in those smears were intermediate cells, but parabasal cells were also seen in some smears (9).

Two smears prepared from histopathologically confirmed squamous cell carcinoma were inadequate. One of them was from the inferior surface of the tongue where the lesion was very fragile and less pressure was applied in taking the smear and the other from the right buccal mucosa close to the retromolar area, a difficult area to reach with the spatula.

There were 02 false negative smears and one of them was from the vermilion border of the lip and the other from the hard palate. The reasons for this may be presence of a thick keratin layer in the lip and the hard palate which is lined with masticatory mucosa to form a protective barrier and less shedding of cells from it as stated by Ogden et al. (8).

One false positive case was reported as squamous cell carcinoma, but histopathologically it was lesion with severe epithelial dysplasia. This finding may be due to misinterpretation by the author because the relevant smear taken by the cytobrush had been diagnosed as severe dyskaryosis.

The results obtained with the uses of spatula technique showed a poor degree of compatibility in the diagnosis of dysplasia and dyskaryosis, similar to the findings reported by Ramesh et al.(9). This poor degree of compatibility may be due to:

Poor cell harvest gained by the use of cytology technique. Only the superficial cell layers are removed with few or no deeply placed epithelial cells. Overlapping and clumping of the epithelial cells on a smear causes difficulty in interpretation of a smear and as the spatula is non-flexible, smears taken from most of the inaccessible sites of the mouth had only a few epithelial cells for a diagnosis. Use of Cytobrush technique In smears prepared by the use of cytobrush, the total number of cells present in a smear were very much higher than that of a smear prepared by the spatula technique. In addition to that, in more than 80% of the smears, parabasal cells could be identified.

Out of the two inadequate smears, one smear was taken from the inferior surface of the tongue and the other was from the left lip and commissure. As the lesion in the inferior surface of the tongue was very fragile, less pressure was applied over the lesion in taking smears and the thick keratin layer forming a crust over the lesion on the lip may be the cause for inadequacy as there is less epithelial cell exfoliation of the lip and the commissure as reported by Folsom et al. (10).

No false negative cases were reported when using the cytobrush technique in our study. But Scuibba (3) reported two inadequate smears in his study of 298 patients.

The compatibility of dysplasia and dyskaryosis was high in our study with the use of the cytobrush technique. This high degree of compatibility of dysplasia and dyskaryosis and the zero false negatives obtained may be due to the good cell harvest gained by the presence of large number of bristles in the brush, touching a larger surface area of the lesion. The number of cells coming from the deeper cell layers was more and less clumping and less overlapping resulted in more accurate microscopical interpretation. As the cytobrush was somewhat flexible, smears taken from most of the inaccessible sites of the mouth had an adequate number of cells for the diagnosis.

Exfoliative cytology of oral leukoplakia

Spatula technique

Four smears were inadequate and according to their site of lesion, one lesion was from the inferior surface of the tongue close its base, one from the alveolar ridge and two were from the left buccal mucosa. The reason for this may be the lesions found on the inferior surface of the tongue and the alveolar ridge was both inaccessible to the spatula and the thick keratin layer over the lesions. A similar type of poor cell yield was also reported by Ogden et al. (8) from smears taken from ventral surface of the tongue.

The inadequacy of the two smears taken from the right and left buccal mucosa may be due to the presence of thick keratin layer over the lesion preventing exfoliation of cells.

Five smears were diagnosed falsely as keratotic; three of them came from the buccal cheek and one each from the right and left commissure. Again the presence of thick keratin layer may have interfered with the exfoliation of deeply placed epithelial cells or the dysplastic change confined to the deeper layers may be the cause for incorrect diagnosis.

Five smears were diagnosed falsely as normal smears. According to their location, 02 smears were from right commissure and one each from the lip, hard palate and dorsum of the tongue. In the commissure, the lip and the dorsum of the tongue, the thick keratin layer may have prevented the exfoliation and the thick masticatory mucosa over the hard palate might be the reason for false negative smear from the hard palate. In this instance atypical cells may be lying in the lower strata or the dysplastic change may be confined to the deeper layers.

One smear was diagnosed falsely as an inflammatory lesion that was taken from the bucco-alveolar sulcus. Therefore, 11 lesions gave false negative results in our study. These false negatives may be due to the presence of thick keratinized layer impeding the emergence of deeper keratotic cells as stated by Mehta et al. (11). Removal of the superficial keratotic layer as much as possible before taking a smear from a lesion and proper selection of the area to harvest may be the reasons for the low false negative rate in our study as compared to the previous studies.

The degree of dyskaryosis of the smears and the degree of dysplasia of the histology were not closely compatible, a finding similar to this was also stated by Ramesh et al. (09). The reasons for this disparity may be the reasons described previously under the use of spatula technique in the diagnosis of oral squamous cell carcinoma. One mild epithelial dysplasia lesion was diagnosed as squamous cell carcinoma by the use of spatula technique. This may be due to the following; the biopsy tissue might have not been taken from the representative area of the lesion leading to a negative result, only a small segment of the lesion has undergone malignant change, and unless multiple biopsies are taken, the malignant component could be missed. On the other hand, the smears permit sampling of the entire lesions enabling even a small focus of malignancy to be picked up. Thirdly, a technical error occurring in sectioning of the biopsy tissue.

In interpreting cytological smears, subjectivity is a common problem (12). To overcome this problem, inter-observer variation study was done and we found a good agreement of the results among three observers similar to the agreement of grading of dysplasia reported by Lippman et al. (1993).

In our study, the overall diagnostic accuracy of spatula technique in the diagnosis of oral leukoplakia was over 80%. However, in most of studies conducted by various authors, the sensitivity of cytological diagnosis of atypia in leukoplakia were poor. Nevertheless, the studies conducted by Ramesh et al. (09) (92%) and Banoczy (13) (90%) showed a high degree of diagnostic accuracy than the previously mentioned studies.

In our study, taking smears from ulcerated or fissured areas and scraping out the superficial surface before taking a cytological smear may be the reason for the high accuracy of this technique in the diagnosis of leukoplakia lesions. The other reason may be that in 50% of the samples, cytobrush was used to take the first smear and then the second smear was taken by the spatula technique. Therefore, when the smear was attempted for the second time from the same site, the second smear would have harvested more cells from deeper cell layers.

Cytobrush technique

None of the smears was reported as inadequate, but two smears gave false negative results. One cytological smear taken from the right commissure contained only the superficial anucleated squames cells and the other taken from the alveolar ridge showed chronic inflammatory cells. In the former, the thick keratin layer may be the reason for the false negative result and in the latter inability to reach the lesion using the cytobrush may be the reason.

Comparative study of cytobrush and spatula in the diagnosis of precancerous and cancerous lesions

Evaluation of cytological diagnosis of oral squamous cell carcinoma

(a) Spatula technique

Spatula technique is a highly sensitive in the diagnosis of dyskaryosis in clinically malignant lesions but its accuracy and specificity is poor.

Spatula technique is not a sensitive and accurate method in the diagnosis of oral squamous cell carcinoma in clinically malignant lesions. However it can be used to differentiate non-cancerous lesions from cancerous lesions in clinically malignant lesions.

There are several reports attesting to the sensitivity of cytological diagnosis of clinically malignant lesions of the mouth and oropharynx (Montgomerry and Von Haam 1951, Pomeranz and Stahl 1953, Peters 1958, Sandler and Stahl 1958 and Sliverman et al. 1958 with sensitivity ranging from 86.7 per cent to 94.5 per cent. But in all of these studies cytologically diagnosed dyskaryotic and cancer smears were grouped as true positives. Therefore, it is difficult to compare these findings with the results of our study.

(b) Cytobrush technique

In the diagnosis of dyskaryosis and squamous cell carcinoma in clinically malignant lesions, cytobrush technique is a sensitive and accurate method. These findings are similar to those of Remmerbach et al. (14).

Evaluation of cytological diagnosis of leukoplakia

(a) Spatula technique

Spatula technique is not a highly sensitive technique to diagnose carcinomatous lesions in leukoplakia, but it is good to separate out non-cancerous lesions in leukoplakia.

However, spatula technique is a sensitive and accurate method to differentiate dyskaryotic lesions from the cancerous lesions.

The accuracy of exfoliative cytology in the diagnosis of oral leukoplakia was different from 36.1% stated by Mehta et al. (11) to 90% stated by Banoczy (13). But very recently Mishra et al. (5) reported a good agreement between cytology and histopathological diagnosis in 86.2% of dysplastic lesions and 95.2% in malignant lesions. However, in most of the previous studies done by various authors, dysplastic and cancerous lesions were grouped together as true positives. Therefore, it is difficult to compare their finding with the results of our study.

(b) Cytobrush technique

Cytobrush technique is a sensitive, specific and accurate method in the diagnosis of squamous cell carcinoma and dyskaryosis in leukoplakia. It is difficult to compare the results of this study with results of the previous studies done by various authors as they have grouped both dysplastic and cancerous lesions together as true positives.

Evaluation of the diagnostic ability of spatula and cytobrush techniques in differentiating non-cancerous and non-dysplastic lesions from cancerous and dysplastic lesions

Leukoplakia

(a) Spatula technique

When the spatula technique was used to differentiate cancerous and dysplastic lesions from non-cancerous and non-dysplastic lesions, no statistically significant difference was reported. Therefore, the spatula can be used to differentiate cancerous and dysplastic lesions from non-cancerous and non-dysplastic lesions in leukoplakia. If the test is positive, the final diagnosis will be very accurate. However, it is not the same when the results are negative.

(b) Cytobrush technique

When the cytobrush technique was used to differentiate cancerous and dysplastic lesions from non-cancerous and non-dysplastic lesions, there was no statistically significantly difference with those of histopathological diagnosis. This suggests that the cytobrush can be used to differentiate cancerous and dysplastic lesions from non-cancerous and non-dysplastic lesions in leukoplakia. Therefore, unlike in the case of spatula both positive and negative test results lead to a much reliable diagnosis with the use of cytobrush.

But in a previous study done by Poate et al. (2004) to investigate the uses of cytobrush technique in the diagnosis of oral epithelial dysplasia in potentially malignant lesions a sensitivity of 71.4%, specificity of 32%, PPV of 44.1% and NPV of 60% was reported.

Scheifele et al. (2004) using oral CDx technique reported a high sensitivity (92.3%) and specificity (94.3%) figures in their study on detecting dysplasia and oral squamous cell carcinoma in premalignant lesions were similar to our results.

Squamous cell carcinoma

(a) Spatula technique

When the spatula technique was used to differentiate cancerous and dysplastic lesions from non-cancerous and non-dysplastic lesions, only the specificity was significantly different. Therefore, the spatula technique does not appear to differentiate cancerous and dysplastic lesions from non-cancerous and non-dysplastic lesions in clinically malignant lesions. Therefore, if the test is positive, 98.46% positive test results are either dysplastic or cancerous. However, if the test is negative, only a 50% of the test results are true negatives.

According to the previous comparative studies done by Peters (15) to Ramesh et al. (9), the calculated values of sensitivity, specificity, accuracy, positive predictive value vary and negative predictive value are similar to our study except the finding for specificity which is only 50%. That may be due to 11 false negatives reported in our study.

(b) Cytobrush technique

When the cytobrush technique was used to differentiate cancerous and dysplastic lesions from non-cancerous and non-dysplastic lesions, no statistically significant difference was reported. Therefore, the cytobrush can be used to differentiate cancerous and dysplastic lesions from non-cancerous and non-dysplastic lesions in oral carcinoma. Therefore if the test is positive, all the positive test results are either dysplastic or cancerous and if the test is negative all the negative results are non-cancerous or non-

dysplastic. According to the study done by Scuibba (3), cytological diagnosis of clinically malignant lesions by the use of cytobrush technique, sensitivity, specificity, accuracy, positive predictive value and negative predictive value were 100%, 92.86%, 95.3%, 87.93% and 100% respectively.

According to the above findings of our study, cytobrush is a good cytological instrument for the diagnosis of both oral premalignant and malignant lesions as it is a very simple, user friendly and less time consuming procedure compared to more time consuming quantitative exfoliative cytology techniques or highly expensive molecular biology techniques. As stated by Henry et al. (1960), the greatest value of cytological examination lies in its ability to disclose the presence of intra-epithelial or non-invasive carcinoma when the clinical appearance is relatively innocent and cancer is not suspected. Its utilization prior to biopsy provides greater assurance of definitive diagnosis, as cancer cells can be detected in the cytological smear even though the biopsy specimen may be inadequate for a diagnosis. Moreover, the diagnosis of oral cancer at an earlier stage can improve the prognosis as stated by Epstein in 1992. It is also beneficial in certain clinical situations where the other diagnostic techniques are impractical to use such as when the patient is medically compromised or has received radiotherapy or may be refusing to under go a biopsy (16) or in an anxious patient who insists on, having a treatment for an apparently innocuous lesion, to use as a screening method in patients who have been treated for oral cancer. In a case of multiple mucosal lesions, exfoliative cytology can be used to locate the most appropriate area for the biopsy. If the lesion is located in a region that presents a surgical risk, then the exfoliative cytology is beneficial to come to a diagnosis.

But some disadvantages are also there like only the individual cells could be studied (Therefore, the pathognomonic features of the disease must be present in or on the cells themselves), furthermore only surface epithelial cells can be obtained (Hence, characteristic pathological changes must extend to the surface for accurate diagnosis), cells cannot be studied in their proper tissue relationship to one another as in surgical biopsy specimens. If the surface of the lesion is heavily keratinized, a typical character of the lesion will not be demonstrated. Treatment cannot be predicted on a positive smear. White lesions can be produced by many diseases other than the cancer (Those white lesions are not precancerous. They cannot be diagnosed from exfoliated cells and even though the technique is simple, if not accomplished adequately then the material is not representative, giving an inadequate sample.

Conclusions

According to our findings, the cytological diagnosis of clinically malignant lesions and premalignant lesions by the cytobrush technique is accurate. But, as it gives no information about the presence or extent of invasion, it should not replace the routine histopathological examination. As stated by Umiker et al. (7), the major role of exfoliative cytology is a supportive one for the histopathological examination.

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