Acta Scientific Dental Sciences (ISSN: 2581-4893)

Volume 5 Issue 3 March 2021

Research Article

The Efficacy of Lugol's Iodine Solution in Detecting Dysplasia and Carcinoma *in Situ* Around Oral Cancerous and Precancerous Lesion and its Impact on the Marginal Clearance: A Comparative Study

Abhishek Kumar Singh[1], Krishna Kishor[2]*, Dayashankara Rao JK[3], Rahul Kashyap[4], Pradeep Das[1] and Heera[5]

[1]Consultant Oral and Maxillofacial Surgeon, Oral and Maxillofacial Surgery, Patna, India

[2]Senior Lecturer, Department of Oral and Maxillofacial Surgery, Buddha Institute of Dental Sciences and Hospital, Patna, India

[3]Associate Professor, Head of Department, Oral and Maxillofacial Surgery, College of Dentistry, Qassim University Buraida, Al Qassim Region, Saudi Arabia

[4]Professor, Department of Oral and Maxillofacial Surgery, ITS Dental College, Muradnagar, UP, India

[5]Consultant Oral and Maxillofacial Pathologist, Oral and Maxillofacial Pathology, Patna, India

***Corresponding Author:** Krishna Kishor, Senior Lecturer, Department of Oral and Maxillofacial Surgery, Buddha Institute of Dental Sciences and Hospital, Patna, India.

Received: January 06, 2021

Published: February 16, 2021

Abstract

Background and Objective: Despite good prospect of early diagnosis small developing lesions often go unrecognised. 60% of lesions are well advanced by the time of discovery. The aim of the study was to evaluate the efficacy of Lugol's Iodine in detecting the presence of Dysplasia or Carcinoma *in situ* at the margins of oral cancerous and precancerous lesions. And to evaluate the difference in resected margins between Lugol's stained and unstained lesions.

Materials and Methods: The study comprised 2 groups (10 patients in each) and were selected according to clinical TMN staging. In intervention group Staining of the lesions was done with Lugol's Iodine before resection. Control group was without vital staining. After 1-2 min, stained margins were resected with a safe margin of 1 cm away from the lesion. The tumor along with the resected margins were measured and sent for histo-pathological examination.

Results: The results showed a statistically significant difference between 2 groups in antero-posterior as well as superio-inferior dimensions with the application of lugol's iodine.

Conclusion: We concluded that the study seems to suggest the effectiveness of the Lugol's Iodine stain as an inexpensive adjunct in intra-operative Oral squamous cell margin identification. It hardly takes 5 minutes for application and stain uptake by the tissues.

Keywords: Lugol's Iodine; Squamous Cell Carcinoma; Dysplasia

Introduction

Among various diseases affecting the oral cavity, the predominant mortality rate is of oral cancer worldwide. It is however surprising that even the oral cavity, which is most accessible for daily self examination, is by default a leading cause of death [1]. Oral can-

cer is often preceeded by specific lesions and conditions that have traditionally been called oral potentially malignant condition and lesions. The high incidence of oral cancer and oral potentially malignant disorder in India has long been linked with the habit of betel quid and tobacco chewing .In India, oral cancer constitutes 12% of all the cancers in men and 5% of all in women [2]. The tongue, alveolus gingivobuccal sulcus, buccal mucosa are some of the common sub sites of oral precancer and cancer. The extent of disease using physical observation that combine tactile assessments of the thickness and turgor of the lesion with its visual qualities such as white or red color, ulceration or exophytic growth. Awareness of specific pattern of tumor extension combined with these observations to guide resection with an appropriate "margin" of "normal" tissue [3]. There is sufficient evidence that visual inspection alone is not adequate to differentiate oral cancer from benign lesions [4]. Lugol's iodine, also known as Lugol's solution, first made in 1829, is a solution of elemental iodine and potassium iodide in water, named after French physician Lugol (1786-1851). This solution is often used as antiseptic and disinfectant, as reagent for starch detection in routine laboratory and medical tests. Lugol's iodine is applied on the suspicious lesions, the normal mucosa stains brown or mahogany due to high glycogen content, while dysplastic tissue doesnot stain, and appears pale compared to the surrounding tissue [5].

Materials and Methods

- After the clearance of ethical committee the study was conducted in Department of Oral and Maxillofacial Surgery, Faculty of Dental Sciences, SGT University, Gurgaon,
- The study included 2 groups of patients (10 each).
- Group 1 consist of patients underwent the intervention by staining of the lesions with Lugol's Iodine before resection and was called in Intervention group.
- Group 2 consist of patients underwent standard resection without vital staining and was called in Control group.

Aims and Objective

The present study is conducted to

- Describe the efficacy of Lugol's iodine solution in detecting dysplasia and carcinoma *in situ* around oral cancerous and precancerous lesion and its impact on the marginal clearance.
- To evaluate efficacy of Lugol's iodine to detect synchronous invasive carcinoma.

Intra-operatively

- Examination of lesion followed Photograph.
- Irrigation of the oral cavity with saline, clean the area and then allow to dry.
- Irrigation of the lesion and its surrounding areas with Lugol's Iodine solution for 10-20 seconds. Lugol's iodine being glycophilic was taken up easily by the normal non-cancerous dysplastic tissue which is rich in glycogen. The application was repeated until the parakeratinised stratified squamous epithelium remote from the tumor took up the stain.
- Wait for 1-2 min (till the stain is taken up by the normal mucosa).
- Interpretation of the stain reaction followed by Photograph.
- The margins stained by the Lugol's Iodine solution are demarcated using incision placed by no 15 BP blade and was resected with a safe margin of 1 cm away from the stained tissue adjacent to the lesion.
- Neck Dissection was done according to the nodal status.
- The tumor along with the resected margins was measured and sent for histo-pathological examination. The stained epithelium was then examined for dysplastic changes. Standard histo-pathological analysis protocols were followed for the operated patients. Histo-pathological margins of the excised specimen was examined for presence or absence of invasion by lesion or dysplasia.

Figure 1

Duration of study

Six months follow-up study with post-operative histo-pathological analysis was performed.

Statistical analysis

Descriptive statistical analysis was used to compare demographics and to evaluate these parameters using Pearson $\chi 2$ test and *p*-values were calculated to establish the significance level.

- Results and observations A total of 20 patients were operated with age ranging from 30 to 80 years with mean age of 58+_8 years.
- Site of primary tumour 20 SITE of primary tumour were recorded in 20 patients Out of 20 primary tumours, 5 patients accounts primary site as Buccal mucosa, lip 04, GBS 05, Alveolus 02, Tongue 04.

T stage distribution

In group I

Tumour staging	No of patients
T1	3
T2	3
T3	2
T4	2

Table a

In group II

Tumour staging	No of patients
T1	2
T2	2
T3	3
T4	3

Table b

Quantification of lesions antero-posteriorly in lugol's stained group (Group 1)

The mean Antero-posterior dimension in group I of 10 patients which was 2.8cm. After application of Lugol, the mean dimension was 3.4cm, while the mean Antero-posterior dimension of the resected specimen was 4.5cm. This shows that the difference in mean between the original lesion and the lesion after stains was 0.6cm. While the difference in the mean between the resected specimen and the original lesion was 1.7 cm.

Quantification of lesions antero-posteriorly in unstained group (Group 2)

The mean antero-posterior dimension in group II patient (unstained group) was 3.6cm, while the mean antero-posterior dimension of the resected specimen was 4.7cm which is showing a difference in the mean of 1.1cm.

Comparison between ant posterior margins in lugol stained and unstained group

Ant Posterior	Mean ± SD	t value	p value
Stained	1.61 ± .47	3.46	.003
Un stained	1.08 ± .10		

Table c

Since p value is less than 0.05 i.e significance difference between stained and unstained group.

Quantification of lesions superio-inferiorly in lugol's stained group (Group 1)

The mean Superior-inferior dimension in group I of 10 patients which was 2.6cm. After application of Lugol, the mean dimension was 3.0cm, while the mean Superior-inferior dimension of the resected specimen was 4.0cm.This shows that the difference in mean between the original lesion and the lesion after stains was 0.4cm. While the difference in the mean between the resected specimen and the original lesion was 1.4 cm.

Quantification of lesions superio-inferiorly in unstained group (Group 2)

The mean Superior-inferior dimension in group II patient (unstained group) was 3.1cm, while the mean superior-inferior of the resected specimen was 4.2cm which is showing a difference in the mean of 1.1cm.

Comparison between sup-inferior margins in lugol stained and unstained group

Sup-inferior	Mean ± SD	t value	p value
Stained	1.45 ± .51	2.23	.030
Un stained	1.08 ± .14		

Table d

Since p value is less than 0.05 i.e. significance difference between stained and unstained group.

Mean quantification comparison between anterio-posterior and superio-inferior stained and unstained groups respectively

The difference of anterio-posterior mean between lugol's stained and unstained group is 0.6 cm and the superio- inferior difference between lugol's stained and unstained group is 0.3cm (Table 1).

	Lugol's stained	Unstained
Mean anterio-posterior	1.7	1.1
Mean superio-inferioer	1.4	1.1

Table 1

Marginal status in group 1

In Lugol's stained group of 10 cases the number of free margins was 36, 1 cancerous margin, 2 dysplasia and 1 carcinoma *in situ* margin out of 40 margins (Table 2).

Type	No. Of margins	% of margin
Free	36	90
Cancerous	1	2.5
Dysplasia	2	5
Carcinoma *in situ*	1	2.5

Table 2

Marginal status in group 2

In unstained group of 10 cases the number of free margins is 28, cancerous margin is 2, dysplasia is 6 and carcinoma *in situ* is 4 out of 40 margins (Table 3).

Type	No. of margins	% of margin
Free	28	70
Cancerous	2	5
Dysplasia	6	15
Carcinoma *in situ*	4	10

Table 3

Distribution of recurrence at various sites in group 1

Out of the 20 cases operated for Oral squamous cell carcinoma, in 10 cases under Lugol's stained group, there were 8 cases with no recurrence where as 1 case with recurrence at primary site and 1 case with recurrence at secondary site.

Distribution of recurrence at various sites in group 2

Out of the 20 cases operated for Oral squamous cell carcinoma, in 10 cases under unstained group, there were 7 cases with no recurrence where as 2 case with recurrence at primary site and 1 case with recurrence at secondary site.

Discussion

Oral cancer is the Sixth most common cancer among all malignancies globally [6], however in India Oral cancer is the Third most common cancer [7]. 57.5% of the head and neck cancers occur in Asia. The incidence in India is a worrisome 30%. Out of these 60-80% present with advanced disease [8].

In the present study the mean age of the cases was found to be 55±8.34 years. The minimum age was 35 years and maximum was to be 75 year, in contrast with the study of Kulkarni M R., *et al.* [8] who gave an incidence of age ranging 15-49 years with mean age of 34 years.

In our study, Buccal Mucosa emerged as the most common site of occurrence for Oral squamous cell carcinoma (25%), followed by Gingivo Buccal Sulcus (20%) and lateral aspect of tongue as the least commonly occurring site occurrence for Oral squamous cell carcinoma.

These regional variations may be ascribed to the exclusive use of tobacco chewing in Indian population as compared to smoking in western countries. In an epidemiological study conducted in 2013 by Kulkarni M R., *et al.* [8] revealed nearly 2/3rds of the malignancies present in the Indian population was found to be in the bucco-gingival sulcus, which is similar to our study.

In our study out of 20 cases, 10 cases are kept under Lugol's stained group (group 1) while on other 10 were in unstained group allocated randomly to each group. The t-staging of the cases in group 1 and 2 were almost consistent. this helped reduce any bias for calculation of results.

This study was conducted to evaluate the usefulness of one such stain vizLugol's Iodine stain in an attempt to identify the true margins (inclusive of dysplasia) in squamous cell carcinoma.

In our study we compared the clinical and histopathological anterior-posterior and superior-inferior measurements of lesion

of lugol's stained and unstained group separately. Here, we used the Lugol's Iodine to identify the squamous cell carcinoma margins intra-operatively to reduce errors in judgement made by clinical assessment.

The mean antero-posterior dimension in group I patients, the lesion in 10 patients which was 2.8cm. After application of Lugol, the mean dimension was 3.4cm, while the mean antero-posterior dimension of the resected specimen was 4.5cm. This shows that the difference in mean between the original lesion and the lesion after stains was 0.6cm. While the difference in the mean between the resected specimen and the original lesion was 1.7 cm. The safety margin of the resection (wide excision) was considered from the stained margin rather than the visible margin.

The mean antero-posterior dimension in group II patient (unstained group) was 3.6cm, while the mean antero-posterior dimension of the resected specimen was 4.7cm which is showing a difference in the mean of 1.1cm. The margin of wide excision was considered from the visible margin of lesion.

The mean superior-inferior dimension in group I patients, the lesion in 10 patients which was 2.6cm. After application of Lugol, the mean dimension was 3.0cm, while the mean superior-inferior dimension of the resected specimen was 4.0cm. This shows that the difference in mean between the original lesion and the lesion after stains was 0.4cm. While the difference in the mean between the resected specimen and the original lesion was 1.4 cm. The safety margin of the resection (wide excision) was considered from the stained margin rather than the visible margin.

The mean superio-inferior dimension in group II patient (unstained group) was 3.1cm, while the mean superio-inferior of the resected specimen was 4.2cm which is showing a difference in the mean of 1.1cm. The margin of wide excision was considered from the visible margin of lesion.

The difference in the mean from 2 groups were analysed and compared and the results showed a statistically significant difference between 2 groups in both antero-posterior as well as superio-inferior dimensions.

This means that with the application of lugol's iodine we were able to resect more tissue than the visible tumours that showed evidence of dysplasia/ carcinoma in-situ/ squamous cell carcinoma.

Through this study, we analysed, at resected margins equally in both the groups which according to four margins (anterior, superior, posterior and inferior) per lesion meant a total of 40 margins in both groups respectively. In lugol's stained group of 10 cases the number of free margins was 36 and 4 positive margin that is 1 cancerous margin, 2 dysplasia and 1 carcinoma *in situ* out of 40 margins which is shown in table 10, where as in unstained group of 10 cases the number of free margins is 28 and positive margins is 12 that is 2 cancerous margin, 6 dysplasia and 4 carcinoma *in situ* out of 40 margins, as shown in table 1. Where in there was total lack of dysplasia on the stained epithelium. Thus providing staining in 90 % of the cases, with sensitivity of 0.9.

The different analysis of margins showed more number of positive margins in unstained (group 2) when compared to Lugol's stained group (group 1). This shows that had we not used LUGOL'S iodine solution in group 1 patients, the chances of leaving the tumor behind and getting more positive margins would have been more showing incomplete resection. Thus the use of Lugol's iodine solution helped to clear more diseased tissue efficiently and as the results showed the statistically significant difference between two groups.

Nagaraju K., *et al*. (2010) conducted a study on diagnostic efficiency of Lugol's iodine in oral premalignancies which showed the overall sensitivity of Lugol's iodine was 0.92 [9].

In present study, out of 10 cases under Lugol's stained group, there were 9 cases with no recurrence where as 1 case with recurrence at primary site and 1 case with recurren Sce at regional site. In unstained group of 10 cases, there were 7 cases with no recurrence, where as 2 cases with recurrence at primary site and 1 case with recurrence at regional site is occurred. This shows the local recurrence rate in our study is more in unstained group than the Lugol's stained group.

Conclusion

Our study highlights the effectiveness of the vital stain Lugol's Iodine as an inexpensive adjunct in intra-operative Oral squamous cell margin identification, The stain has sensitivity of 97.5%. This stain can be used to aid the surgeon in planning the resection margin as it hardly takes 5 minutes for application and stain uptake by the tissues. With advanced methods like, immunofluorescence, navigation surgery and molecular target agents, the future holds immense promise in improving the accuracy with minimal errors

to map the surgical resection margins. The objective however remains the same i.e. to prevent loco-regional recurrence and to improve the overall survival rates in oral cancer.

Funding

No funding received.

Bibliography

1. Torre L., *et al*. "Global cancer statistics". *Cancer Journal for Clinicians* 65.2 (2012): 87-108.
2. Delilbasi C., *et al*. "Prevelance of oral precancerous lesions in a selected Turkish population". *Turkish Journal of Medical Sciences* 33 (2003): 39-42.
3. Wayne M Koch. "Molecular assessment of surgical margins". Head and Neck Surgery. Johns Hopkins university School of Med (2003): 522-533.
4. Rosenberg D and Cretin S. "Use of meta-analysis to evaluate tolonium chloride in oral cancer screening". *Oral Surgery, Oral Medicine, Oral Pathology* 67.5 (1989): 621-627.
5. Petruzzi M., *et al*. "Use of Lugol's iodine in oral cancer diagnosis: An overview". *Oral Oncology* 46.11 (2010): 811-813.
6. Lingen M., *et al*. "Critical evaluation of diagnostic aids for the detection of oral cancer". *Oral Oncology* 44 (2008): 10-22.
7. Coelho K R. "Challenges of oral cancer burden in India". *Journal of Cancer Epidemiology* (2012).
8. Kulkarni M R. "Head and neck cancer burden in India". *International Journal of Head and Neck Surgery* 4.1 (2013): 29-35.
9. Nagaraju Kamarthi., *et al*. "Diagnostic Efficiency of Toluidine Blue With Lugol's Iodine In Oral Premalignant And Malignant Lesions". *Indian Journal of Dental Research* 21.2 (2010): 218.