

Special care for oral tissue samples after biopsy: Proper storage and transport – A comparative Study

Cuidado especial para las muestras de tejido bucal después de la biopsia: Almacenamiento y transporte adecuados – Un estudio comparativo.

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Abstract: Objective: Biopsy is the gold standard for the diagnosis of oral lesions. Correct management and care of biopsy at all steps (before, during and after obtaining a biopsy) is highly important to provide proper tissue samples for microscopic assessment by pathologists. This study aimed to assess and compare the knowledge of dental students (DSs) and general dentists (GDs) on post-oral biopsy instructions. **Material and Methods:** A questionnaire including two parts was used:

1) Demographic data and self-evaluation of biopsy knowledge by the participants and

2) 11 items about the correct oral biopsy storage and transport to a histopathology laboratory. The data collected from the questionnaires were analyzed by STATA. **Results:** 48 GDs and 131 DSs participated in this study. The knowledge score of the DSs (5.43 ± 2.01) was significantly lower than GDs (8.33 ± 1.78) ($p < 0.05$). Moreover, there was no significant relationship between GDs' knowledge and their working experience, age, gender and the university they graduated from. However, there was a significant relationship between DSs' school year and their knowledge.

Conclusion: The findings showed that the knowledge of DSs was lower than GDs. Since, these students will care for the oral and dental health of the community in the future, upgrading their training (by improving the quantity and quality of theoretical and practical training) is necessary to both understand the different aspects of biopsy, and to be familiar enough with proper oral biopsy storage and transport processes.

Keywords: Knowledge; biopsy; students, dental; dentists; Mouth Neoplasms; Surveys and Questionnaires.

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Resumen: Objetivo: La biopsia es el estándar de oro para el diagnóstico de lesiones bucales. El manejo y cuidado correctos de la biopsia durante todos los pasos (antes, durante y después de obtener una biopsia) es muy importante para proporcionar muestras de tejido adecuadas para la evaluación microscópica por parte de los patólogos. Este estudio tuvo como objetivo evaluar y comparar los conocimientos de estudiantes de odontología (SD) y dentistas generales

(GD) sobre las instrucciones posteriores a la biopsia oral. **Material y Métodos:** Se utilizó un cuestionario que constaba de dos partes:

1) Datos demográficos y autoevaluación del conocimiento de la biopsia por parte de los participantes y

2) 11 ítems sobre el correcto almacenamiento y transporte de la biopsia oral a un laboratorio de histopatología. STATA analizó los datos recopilados de los cuestionarios.

Resultados: 48 GD y 131 SD participaron en este estudio. La puntuación de conocimiento de los DS ($5,43 \pm 2,01$) fue significativamente menor que la de los GD ($8,33 \pm 1,78$) ($p < 0,05$). Además, no hubo una relación significativa entre los conocimientos de los GD y su experiencia laboral, edad, género y la universidad de la que se graduaron.

INTRODUCTION.

Any abnormality in oral cavity should be biopsy, particularly if it persists for more than 2 weeks even after removing the possible irritating factor(s).¹ Biopsy is the gold standard modality for the definitive diagnosis of oral pathologies.^{1,2} This term is defined for obtaining a tissue sample from a living organism for microscopic evaluation.^{1,3} Correct management and care of biopsy at all steps (before, during and after taking a biopsy) is highly important^{2,4,5} to provide proper tissue sample for microscopic assessment by pathologists.^{4,5}

Therefore, the clinicians should strictly follow the available protocols and instructions during the entire procedure of obtaining a biopsy, including post-biopsy instructions such as correct fixation and storage of sample, proper handling and transport as well as providing the pathologist with complete and accurate clinical information about the lesion.^{1,4,5}

Given that the clinicians have an important role in proper management and care of biopsy samples in order to come up with a correct diagnosis, this study assessed and compared the knowledge of post-oral biopsy instructions between general dentists (GDs) and dental students (DSs) of Kurdistan University of Medical Sciences (Sanandaj city, Iran).

MATERIALS AND METHODS.

This cross-sectional study was conducted using an anonymous self-administered questionnaire which included two parts:

A) Demographic data and self-evaluation biopsy

Sin embargo, hubo una relación significativa entre el año escolar de los DS y sus conocimientos. **Conclusión:** Los hallazgos mostraron que el conocimiento de los SD era menor que el de los GD. Dado que estos estudiantes se ocuparán de la salud bucodental de la comunidad en el futuro, es necesario mejorar su formación (mejorando la cantidad y calidad de la formación teórica y práctica) tanto para comprender los diferentes aspectos de la biopsia como para estar familiarizados suficientemente con los procesos adecuados de almacenamiento y transporte de biopsias orales.

Palabra Clave: Conocimiento; biopsia; Estudiantes de Odontología; odontólogos; Neoplasias de la Boca; Encuestas y Cuestionarios.

knowledge of participants;

B) Eleven items on proper biopsy storage and transport to a histopathology laboratory for routine microscopic/histopathological evaluation and analysis. The validity and reliability of the questionnaire were calculated and confirmed.

The survey was conducted using a census approach. All 180 dental faculty students and 87 GDs working in the city of Sanandaj were invited to participate in this study as a list of the practicing GDs in the city was obtained from the medical council of Sanandaj.

Questionnaires were hand-delivered by a team of two investigators. The questionnaires were collected from the respondents after presenting the study to the participants, obtaining the informed consent and giving sufficient time (approximately 15 minutes) to fill them in. Participation in the study was voluntary so those who were willing to participate were included and were assured of the confidentiality of their responses. After collecting the questionnaires, the knowledge score of each participant was calculated by summing the scores of all answers. Each correct answer received one point score and each incorrect or no response answers were given no score, as such the maximum score was 11 points. This study was approved by the Research Ethics Committee of Kurdistan University of Medical Sciences (approval number IR.MUK.REC.1396.342).

Statistical analysis

Data were analyzed using STATA (version 12) by Mann-Whitney and Kruskal-Wallis tests and Spearman's correlation coefficient, $p < 0.05$ was considered significant.

Table 1. Knowledge score based on DSs school year, work experience of GDs and university of graduation of GDs.

	Variable	N (%)	Knowledge score
School year of Dental students	1 th	22 (16.8)	4.23 ± 1.51
	2 nd	23 (17.6)	4.65 ± 1.69
	3 rd	23 (17.6)	5.43 ± 2.19
	4 th	24 (18.3)	5.92 ± 2.28
	5 th	21 (16.0)	5.86 ± 1.90
	6 th	18 (13.7)	6.72 ± 1.36
University of graduation of General dentists	Tehran	21 (43.7)	8.48 ± 1.78
	Hamadan	20 (41.7)	7.95 ± 1.90
	Tabriz	4 (8.3)	10.50 ± 0.71
	Kerman	2 (4.2)	8.00 ± 0.00
	Shiraz	1 (2.1)	10.00 ± 0.00
Work experience of General dentists	< 10 years	20 (41.7)	8.11 ± 1.81
	10-20 years	23 (47.9)	8.13 ± 1.68
	>20 years	5 (10.4)	9.40 ± 1.95

Table 2. Self-evaluation of biopsy knowledge by DSs and GDs and also sources of such knowledge.

Self-evaluation questions	Answers	Dental students	General dentists
		N(%)	N(%)
Do you have any knowledge on proper biopsy storage and transport?	Yes	51(38.9)	37 (77.1)
	No	80 (61.1)	11(22.9)
If your answer to the above is "Yes" do you evaluate your knowledge to be adequate?	Yes	29 (56.9)	20 (54)
	No	22 (43.1)	17 (46)
What is the source(s) of your knowledge?	Academic Education	33(64.7)	22(59.5)
	Reading Scientific Literature	8(15.7)	7 (18.9)
	Academic Education + Conferences	2(3.9)	4 (10.8)
	Academic Education + Reading Scientific Literature	0(0.0)	3(8.1)
	Academic Education + Reading Scientific Literature+Conferences	1(2.0)	1 (2.7)
	Conferences	2(3.9)	0 (0.0)
	Peers (other students/colleagues)	4(7.8)	0 (0.0)
	Reading Scientific Literature+Conferences	1(2.0)	0 (0.0)

Table 3. Reasons for not sending biopsy samples to histopathological laboratory.

Reasons	Dental students	General dentists
	N (%)	N (%)
Biopsy is not a dentist duty	12 (27.9)	14 (43.7)
Biopsy is not applicable for a patient	2 (6.2)	0 (0.0)
There is no need for histopathological assessment when a lesion is clinically diagnosed	4 (9.3)	0 (0.0)
Lack of patient's consent for biopsy	0 (0.0)	2 (6.2)
Lack of proper academic education/training	24 (55.9)	11 (34.4)
Biopsy is not a dentist duty + Lack of enough education/training	2 (4.6)	0 (0.0)
Others	1 (2.3)	3 (9.4)

Table 4. Frequency distribution of GDs, and DSs, answers to the questionnaire items.

Item	Correct Questionnaire item	Dental students answer		General dentists answer	
		Correct	Incorrect/ no answer	Correct	Incorrect/ no answer
		N (%)	N (%)	N (%)	N (%)
1	Histopathological assessment of each abnormal oral tissue sample taken as biopsy is necessary.	82 (62.6)	49 (37.4)	48 (100)	0 (0.0)
2	The entire lesion/all the tissue piece excised during a biopsy should be sent to histopathological assessment	84 (64.1)	47 (35.9)	26 (54.2)	22 (45.8)
3	The entire lesion/all the tissue pieces excised during a biopsy should be sent to one histopathological laboratory	63 (48.1)	68 (51.9)	42 (87.5)	6 (12.5)
4	The collected biopsy sample should be immediately placed in fixative.	76 (58)	55 (42)	44 (91.7)	4 (8.3)
5	The best fixation method is to immerse the sample in a container containing suitable fixative.	65 (49.6)	66 (50.4)	47 (97.9)	1 (2.1)
6	10-15% buffered formalin is the most suitable fixative for routine histopathological assessment of tissue samples using a light microscope.	66 (50.4)	65 (49.6)	43 (89.6)	5 (10.4)
7	The sample should be immersed in sufficient volume of fixative(10-20 times the volume of sample).	44 (33.6)	87 (66.4)	25 (52.1)	23 (47.9)
8	A plastic container with a wide opening is recommended for sample transfer to laboratory.	41 (31.3)	90 (68.7)	21 (43.8)	27 (56.2)
9	The sample container should have a screw-cap.	58 (44.3)	73 (55.7)	26 (54.2)	22 (45.8)
10	Before sending biopsy to laboratory name of patient, clinician and site of biopsy should be labeled on body of container.	78 (59.5)	53 (40.5)	38 (79.2)	10 (20.8)
11	Recording and sending comprehensive information (such as clinical patient history and clinical/radiographic findings) play important role on correct histopathological interpretation and diagnosis.	54 (41.2)	77 (58.8)	40 (83.3)	8 (16.7)

RESULTS.

A total of 131 out of 180 DSs and 48 of 87 GDs participated in this study voluntarily.

Descriptive results

Of 131 DSs, with a mean age of 23.33±2.98 years old, 85 (64.89%) were male and 46 (35.11%) were female. Also, the highest and the lowest number of DSs were in the fourth (n=24) and sixth (n=18) school years, respectively (Table 1). Self-evaluation of biopsy knowledge by DSs as well as sources of such knowledge is presented in Table 2.

Moreover, 67.2% (n=88) of DSs had positive and 32.8% (n=43) had negative attitudes about sending a biopsy to a laboratory in the future. Table 3 presents the stated reasons for not sending biopsy to the laboratory. DSs knowledge mean score was 5.43±2.01 (ranging from 0

to 10). Table 1 presented the knowledge score of DSs based on their school year. The frequency distribution of DSs responses to each question is also presented in Table 4.

Of 48 GDs, 28 (58.83 %) were male and 20 (41.67 %) were female and their mean age was 39.62±5.75 years old. Their mean years of work experience was 11.93±4.68 years (ranging from 4 to 25 years), and the majority (21, 43.7%) graduated from Tehran University of Medical Sciences (Table 1). Self-evaluation of biopsy knowledge by GDs and sources of such knowledge are presented in Table 2. The findings showed that 66.7% of GDs (n=32) had never sent a biopsy to a laboratory; the reasons are presented in Table 3. GDs knowledge score mean was 8.33±1.78 (ranging from 3 to 11). Knowledge scores of GDs, based on their work experience and the

university they graduated from, are presented in Table 1. Table 4 shows the frequency distribution of responses of GDs to the items.

Analytical results

Kruskal-Wallis test showed that there is a significant correlation between the knowledge score of DSs and their school year ($p < 0.05$). However, the knowledge score of the males (5.62 ± 1.96) and the females (5.74 ± 2.08) DSs were not significantly different (Mann Whitney test, $p = 0.28$). There was no significant correlation between the knowledge score of GDs and the university they graduated from ($p = 0.16$) and the years of work experience ($p = 0.247$). No significant difference was found between knowledge scores of males (8.46 ± 1.81) and females (8.15 ± 1.75) ($p = 0.78$).

On the other hand, Spearman's correlation test showed a significant correlation between age and knowledge score of DSs, so that their knowledge score was significantly increased by an increase in their age (correlation coefficient = 0.235, $p = 0.006$). This correlation was not significant for GDs (correlation coefficient = -0.034, $p = 0.818$).

Comparison of the knowledge score of DSs and GDs showed a significant difference in terms of the correct oral biopsy storage and transport. The knowledge score of GDs in this area was significantly higher than that of DSs (Student t-test, $p = 0.0001$).

DISCUSSION.

Taking a biopsy sample for histopathological study is the most effective strategy to correct diagnosis of oral lesions.⁶ In addition to the errors related to taking a biopsy, delay fixation, use of a fixative solution without considering type of diagnostic technique, improper storage and transport of oral biopsy can also result in an incorrect interpretation by pathologists.^{1,4,5}

In this study a higher percentage of GDs believed that they had knowledge on proper oral biopsy storage and transport compared to DSs. Unfortunately, the difference between the two groups was considerable. This difference, especially in relation to the DS who are still busy with their studies at the university and have the opportunity to acquire more knowledge in this area, was discouraging. However, this finding could be due to the inclusion of DS in lower school years in the study, who had not yet received theoretical and practical training in this area.

The majority of GDs and DSs reported that they

acquired their knowledge during their dental education. Furthermore, not only in the curriculum, but even afterwards, what was taught about biopsy in academic educational settings compared to other sources seemed to be of greater importance and to play a more prominent role. As such, it is important to pay attention to both the quantity and the quality of theoretical and practical training to obviate the educational weaknesses in this area. Taking an oral biopsy sample is a simple surgical procedure,⁷ and all GDs should be able to do it.^{8,9} The majority of GDs reported that they never sent a biopsy sample to the laboratory. However, some stated that taking a biopsy is not the duty of a dentist or that they did not receive any training in this area.

The majority of DSs, who stated that they would not do biopsy in the future, believed that lack of training was the main reason. Murgod *et al.*,¹¹ reported that the main reasons for dentists to not perform a biopsy were patients' lack of consent to the procedure, the dentists' lack of adequate experience/ expertise in this area and not having the required instruments to do the biopsy.¹⁰ On the other hand, Bataineh *et al.* put the greatest emphasis on the absence of adequate training in the dental curriculum.

In the present study, no significant correlation between knowledge of GDs and their work experience, age, gender and the university they graduated from was found. Similarly, Bataineh *et al.*,¹¹ found no significant correlation between the work experience of GDs and their knowledge about biopsy. However, Lopez-Jornet *et al.*,⁹ showed that GDs with a longer work experience were more willing to perform biopsy.

The knowledge score of DSs had a significant correlation with their school year and age. The increasing age of the DSs reflected their more advanced academic development. The knowledge score of the 6th year DSs was higher than that of DSs at lower school years, which could be due to a more comprehensive theoretical knowledge acquisition, increased clinical experience and performing a higher number of biopsy cases compared with DSs still at lower school years. Improper oral biopsy storage and transport could be due to the lack of knowledge in this area.

Therefore, it is vital to perform assessments and to offer the necessary training based on the results. Also, it is necessary to determine the knowledge level of DSs and GDs in order to design the correct curriculum in dental schools to reach this goal.

In this study, the items (correct answers of the questions asked in the questionnaire) were as follows:

1: Histopathological analysis of each abnormal oral tissue sample taken as biopsy is necessary to achieve a final diagnosis.^{3,5}

2 and 3: The entire lesion/all the tissue pieces excised should be sent to one laboratory.¹² Sending only a part of a sample to a laboratory may result in missing of histopathological changes and inaccessibility of pathologist to important microscopically diagnostic features in other parts of the sample (which were not sent to the laboratory). This can lead to controversial diagnoses by different laboratories which can adversely affect the proper management of the disease in the patient.

4: The collected biopsy sample should be immediately placed in fixative.⁴

Delay between tissue collection and its immersion in fixative can result in activation of tissue enzymes, autolysis and protein degradation.¹³ These processes can cause changes in tissue and make it histopathologically undetectable.¹⁴

5: For optimal fixation, the best method is to immerse the sample in a container containing suitable fixative.¹⁵ Wrapping the sample in a gauze, cotton or tissue paper can cause its dehydration and drying and the tissue may remain un-fixed.¹³ Moreover, it would be difficult to separate the dry tissue from the gauze¹⁴ and this may damage it. Freezing the tissue sample, instead of fixing it, is also incorrect since it can cause cellular changes and epithelial perforations due to the formation of ice crystals.^{3,16}

6: At present, 10%-15% buffered formalin is the most suitable fixative solution for routine histopathologic assessment of tissue samples under a light microscope.^{5,16} Biopsy samples immersed in solutions such as water, saline or alcohol often show abnormal cellular and structural changes, which can cause problems in reaching a correct diagnosis.¹⁷ Samples are not properly fixed in these solutions^{3,14} and tissue autolysis continues.¹⁶

7: The sample should be immersed in sufficient volume of fixative to ensure its adequate fixation.¹ The sample should also be submerged in the fixative.¹⁵ This volume varies from 10 to 20 times the volume of sample in the literature.¹⁴ If the sample is not completely immersed in formalin, it may become dehydrated; dehydration confers a dry appearance to the sample and causes

cracking and over-staining of tissue sections.

8: A plastic container¹² with a wide opening¹ is recommended to transfer the sample to the laboratory. Using a glass container is risky since it may break and hurt people. Moreover, small glass particles may penetrate into the tissue sample and damage the microtome used for tissue sectioning.^{12,18}

Formalin also increases the tissue consistency and results in its hardening.¹ The opening of the container used for sample transfer should be wide in order to allow an easy and safe removal of the tissue from the container.

9: The tissue sample container should have a screw-cap.¹² Formalin is classified as a carcinogen.^{19,20} Contact of formalin with skin and breathing its vapor are dangerous for the person who carries the container.²⁰ It seems that press-to-seal containers (such as some injection bottles) have a higher risk of leakage and evaporation of fixative compared with screw-cap containers.

10: All biopsy containers should be labeled.¹⁴ These labels should be stuck to the body of the container, not to the caps.²¹ In the laboratory, after opening the caps of similar containers, there is a possibility of caps misplacing and as a result label misplacing, thus, serious errors may occur. The label should contain the name of patient, the name of clinician and site of biopsy.^{1,14}

Having a label is so important that the laboratory can refuse to accept the containers without proper labeling and send them back to the clinician for correct labeling.^{12,18}

11: Histopathology assessment includes microscopic and macroscopic study of tissue as well as its relation to clinical history and any imaging findings.⁴ Thus, it is necessary to provide the pathologist with comprehensive patient history, information about the lesion and name and address of the clinician in charge of the patient.²²

Such information should be recorded in the histopathological assessment request form 4 and sent to the laboratory along with the biopsy sample.⁴ This form is the first line of communication between the clinician and the laboratory.¹⁸ By doing so, the pathologist gets an idea of what the dentist observed and what they think about the lesion.²³

CONCLUSION.

In this study the knowledge of GDs was significantly higher than that of DSs. However, the knowledge of both groups highlighted the need for further training

programs both before and after graduation.

Considering our small sample size, our results may not be generalizable to the entire population of DSs and GDs in Iran. However, our findings highlighted the need for knowledge improvement in this area.

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Ethics approval: This study was approved by the Research Ethics Committee of Kurdistan University of Medical Sciences (IR.MUK.REC.1396.342).

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