Ukrainian Scientific Medical Youth Journal
Issue 4 (127), 2021
ISSN 1996-353X
ISSN 2311-6951

UDC 616.211-008.4:616.315-018:616-006.52-022.6
https://doi.org/10.32345/USMYJ.4(127).2021.30-37

Received: October 3,2021
Accepted: November 29,2021

MORPHOLOGICAL CHANGES IN SOFT PALATINE TISSUES STANDING BEHIND OBSTRUCTIVE SLEEP APNEA SYNDROME: GENERAL PATTERN AND ROLE OF HUMAN PAPILLOMA VIRUS.

Denysenko Roman[1], Gychka Sergiy[2], Nikolaienko Sofia[2], Dikhtiaruk Oleksandr[1], Naumenko Oleksandr[1]

[1]Department of Otorhinolaryngology, Bogomolets National Medical University, Kyiv, Ukraine

[2]Department of Pathological Anatomy, Bogomolets National Medical University, Kyiv, Ukraine

Abstract: *snoring and obstructive sleep apnea syndrome (OSAS) are a serious medical problem, as they lead to a complex of complications from various body systems, disrupt the socio-economic sphere and stigmatize patients. To date, a set of treatments has been developed, the most effective of which are conservative therapy using CPAP and surgical interventions - various modifications of uvulopalatopharyngoplasty. However, only a small number of studies have elucidated soft palate tissue pathology in patients with chronic and OSAS. But understanding the morphological changes is one of the key aspects for the development of treatment tactics. The aim of current study is to justify the choice of surgical intervention in the treatment of snoring and OSAS by description of morphological changes of the soft palate and to estimate the impact of HPV infection on the progression of soft palatine remodeling. The study included soft palatine tissue samples, which were removed during surgery for snoring and OSAS in 15 patients. Histological (H&E) and immunohistochemical techniques (Ki-67, p16, Human Papilloma Virus). All patients were divided in two groups according HPV-positivity: 5 persons in HPV-positive group and 10 persons in HPV-negative group. For indicators were estimated: number of cellular layers (CL), number of intraepithelial lymphocytes (per 100 epitheliocytes) (IEL), number of vessels per x100 field (NV), Ki-67 proliferation index (PI). Results shows in HPV+ group: CL - 24,2 (±2,17); IEL - 37,8 (±20,97), NV - 21 (±8,46); PI - 17,6 (±2,51). In HPV- group: CL - 6 (±4,78); IEL - 3,3 (±1,77); NV - 10,7 (±2,67); PI - 7,3 (±2,71). Mann-Whitney criterion shows statistical significant difference between groups for all mentioned indicators. In conclusion: patients with snoring and obstructive sleep apnea syndrome had hypertrophy of the soft palate structures caused by changes in epithelial and connective tissue components. Subepithelial structures underdo the disorganization of connective tissue components with a violation of the histoarchitectonics of collagen fibers, edema and angiomatosis. Thus, the study revealed a number of irreversible pathological processes of soft palate tissues, which is the basis for the choice of surgical treatment tactics including the resection of excess tissue. At the same time HPV-infection leads to more pronounced changes in the epithelial layer and subepithelial tissue with concomitant inflammation that likely to create a negative background for further treatment of OSA syndrome.*

Key words: soft palate, papillomaviridae, sleep apnea syndromes, viruses, alphapapillomavirus, snoring.

Introduction. Obstructive sleep apnea (OSA) is referring to one of the most prevalent sleep disorders worldwide and is caused by repetitive episodes of nocturnal breathing cessation due to upper airway collapse (Spicuzza, Caruso, & Di Maria, 2015). Frequent and prolonged episodes of OSA leads to the development of obstructive sleep apnea syndrome (OSAS) which includes nocturnal sleep disruptions, decrease in general quality of sleep and consequent excessive daytime sleepiness (Mannarino, Di Filippo, & Pirro, 2012). Clinically, OSAS is manifested by asthenization, decreased efficiency and decreased cognitive abilities. Meanwhile OSAS increases irritability, and together with snoring, leads to a decrease in the quality of life and family problems [3]. Numerous of studies have shown strong correlation between OSAS and different cardiovascular diseases. These include congestive heart failure, arterial hypertension and cerebrovascular disorders (Lévy et al., 2015). Previous studies have shown that patients with untreated severe OSA have a significantly higher risk of fatal (OR) - 2.87) and non-fatal (OR - 3.17) episodes of cardiovascular disease compared with group of healthy people (Lévy et al., 2015).

The golden standard of the therapy of OSAS is CPAP therapy (Constant Positive Airway Pressure) of its main alternative - oral appliances. Randomized clinical trials show similar improvements in health outcomes between these two treatments, including sleepiness, quality of life, driving performance, and blood pressure (Sutherland, Phillips, & Cistulli, 2015). However, according Clinical

ISSN 1996-353X
ISSN 2311-6951

Guidelines for Obstructive Sleep Apnea and Insomnia published in 2020, CPAP is being main therapeutic approach for severe OSA and symptomatic mild-to-moderate OSA. Moreover, individuals with OSA should use CPAP treatment at all times when sleeping (Sutherland et al., 2015). However, CPAP therapy can cause significant physical and psychological discomfort in patients, worsen the process of falling asleep, as well as cause irritation of the skin (Pépin et al., 1995). As a result, a cohort of patients with low compliance with conventional therapy is formed, which requires the use of other therapeutic approaches. Newest guidelines consider three alternatives – already mentioned mandibular advancement devices, hypoglossal nerve stimulation and surgical interventions (Mysliwiec et al., 2020). Among surgical techniques the most prevalent are different modifications of operations on the soft palatine and pharynx – the uvulopalatopharyngoplasty.

Remodeling of oropharyngeal region has shown higher effectiveness in the treatment of OSA syndrome [3]. However, only a small number of studies have elucidated soft palate tissue pathology in patients with chronic and OSAS. D. Friberg et al. have estimated the number of biopsies of palatopharyngeal muscle in patients with and without OSA and shown strong differences in the number of hypertrophied and/or atrophied fibers in patients compared with controls (Friberg et al., 1998). Yongyi Liu and collogues established a rat model to describe histological, ultrastructural, and physiological changes in case of OSA. Authors shown that study group rats had cardiac myocyte disarray, vacuolar degeneration and mitochondrial abnormalities of myocytes (Liu et al., 2019). B. T. Woodson et al. published results of 8 patients with OSA that represent hypertrophy of mucous gland with the dilation of ducts. In addition, there had been found focal squamous metaplasia, disruption and focal atrophy of muscle bundles, extensive edema of the lamina propria with vascular dilation (Mysliwiec et al., 2020).

Even less information has been published on the topic of relation between human papilloma virus (HPV) infection and OSA syndrome. According different studies the prevalence of oral HPV infection varies from 6,9% in USA with the higher prevalence in man (Gillison et al., 2012) and 9,3% in the youth population in Sweden with higher prevalence in woman (Du et al., 2012). Well know typical HPV-related lesions of the epithelium are squamous cell papilloma, verruca vulgaris, condyloma acuminatum and focal epithelial hyperplasia in case of low-risk HPV and leukoplakia, erythroplakia and oropharyngeal squamous cell carcinoma in case on high-risk HPV (Feller, Khammissa, Wood, & Lemmer, 2009). All mentioned changes have common features characterized by hyperplastic, hypertrophic and dysplastic processes. Currently only one broad publication highlights the role of HPV infection in the development on OSA meaning that this topic is still being understudied (Baldwin, Chitale, Chen, Worsham, & Yaremchuk, 2017).

However, the understanding of morphological changes is one of the key aspects for the development of treatment tactics.

The aim of current study is to justify the choice of surgical intervention in the treatment of snoring and OSAS by description of morphological changes of the soft palate and to estimate the impact of HPV infection on the progression of soft palatine remodeling.

Material and methods. The study was conducted at the Departments of Otorhinolaryngology and Pathological Anatomy of the Bogomolets National Medical University from June 2021 to August 2021. The study protocol was approved by the Commission on Bioethical Expertise and Ethics of Scientific Research at Bogomolets National Medical University (Protocol #126 from 13.11.2019). All patients signed an informed consent to participate in the study.

Criteria for inclusion in the study were snoring and OSA stage II (Boudewyns, Marklund, & Hochban, 2007) and low compliance with a history of CPAP therapy. Exclusion criteria were age less than 18 years and more than 75, pregnancy, severe forms of OSA (stage III and above), chronic respiratory diseases - COPD, tuberculosis, bronchial asthma, cancer of any location, severe comorbidities, anesthesia risk on ASA III scale and above, deformation of the frontal part of the skull.

Material for the study was soft palatine tissue samples removed during surgery for snoring and OSAS. For histological examinations, samples of soft palatine tissue were fixed overnight in 10% buffered formalin at room temperature. Fixed tissues were embedded in paraffin. The H&E sections were prepared according standard histological method. Slides were examined using a Leica BX 51 microscope, a Leica MC 190 digital camera, and the Leica LAS software at magnifications of 100×–400×. Immunohistochemical staining was performed to detect expression of Ki-67 (Diagnostic BioSystems Clone SP6), p16 (Diagnostic BioSystems Clone JC2), Human Papilloma Virus (ThermoScientific Clone K1H8). Morphometric investigations included the assessment of severity of hyperplasia and hypertrophy (number of cellular layers and thickness of epithelial layer) of integumentary squamous epithelium, vascularization (number of vessels), severity of subepithelial edema, severity of perivascular and diffuse inflammatory infiltration. For this aim Image J software was used.

Statistical analysis was performed using SPSS IBM Statistics v. 28.0.0.0. Study groups were compared according the values of median ± confidence interval, median, number of positive indicators in group, statistical difference was calculated with non-parametric tests such as Mann-Whitney criterion (for two independent samples).

15 patients were included in the study and divided in two groups according the presence or absence of the HPV-infection (positive expression of anti-HPV antibody during immunohistochemistry). HPV-negative

ISSN 1996-353X
ISSN 2311-6951

Parameter	Values (SD)	Coefficient of variation, %
Age, years	48 (±16,23)	33,8
Sex, number of patients		
Male	11	-
Female	4	-
Weigh, kg	89,4 (±11,34)	12,68
Height, cm	170,63 (±8,91)	5,2
BMI	30,83 (±2,21)	7,17
ASA class, number of patients		
I	7	-
II	8	-

Table 1. General characteristics of the sample.

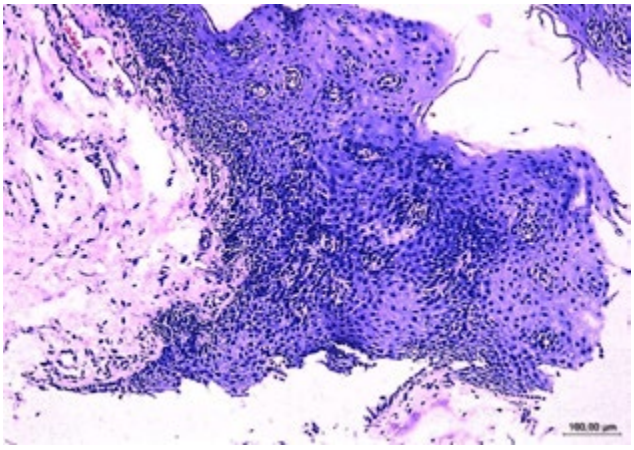


Figure 1. Papillomatous hyperplasia of integumentary squamous epithelium.

group accounted 10 cases, correspondingly HPV-positive – 5 patients.

Results. Table 1 highlights main demographic characteristics of the sample. No statistically significant differences were found between two group though they are not displayed below.

All cases had number of common histological features but in different level of severity. These features were hyperplasia and hypertrophy of integumentary squamous epithelium (including papillomatous); plethora of blood vessels and angiomatosis of the subepithelial connective tissue; edema and disorganization of fibrous structures and mild inflammatory infiltration of subepithelial tissues. Figures 1-4 shows typical histological changes in patients.

Representative hematoxylin and eosin staining image showing papillomatous hyperplasia and low-grade dysplasia of integumentary squamous epithelium. Subepithelial tissues with mild chronic inflammatory infiltration, disorganization and edema of connective tissue. H&E stain, magnification x100.

Representative hematoxylin and eosin staining image showing severe hyperplasia of integumentary squamous epithelium with evenly increased number of cellular layers and dystrophic changes. H&E stain, magnification x100.

Representative hematoxylin and eosin staining image showing hyperplasia of integumentary squamous epithelium, moderate angiomatosis and plethora, moderate chronic inflammatory infiltration of subepithelial tissues and numerous of intraepithelial lymphocytes. H&E stain, magnification x100.

Representative hematoxylin and eosin staining image showing increased number of vessels (angiomatosis), plethora and connective tissue edema with disorganization of connective tissue. H&E stain, magnification x200.

Immunohistochemical study allows to determine the presence of HPV-infection and the activation of oncogenesis processes associated with MTS1 protein (positive reaction p16) (fig. 5-6).

Representative IHC HPV general staining image showing the composed nuclear and cytoplasmic reaction

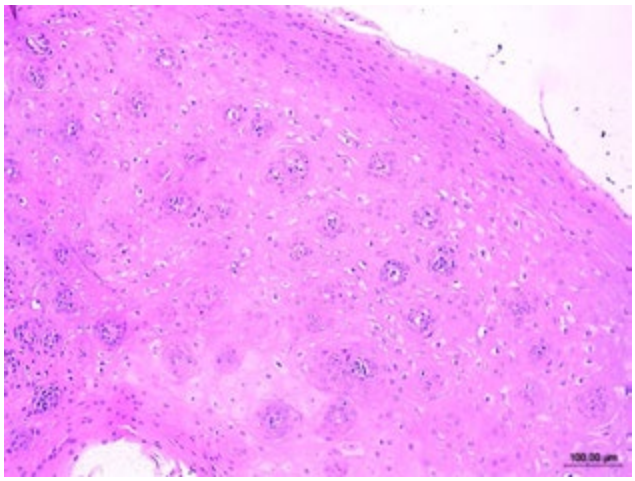


Figure 2. Severe hyperplasia of integumentary squamous epithelium.

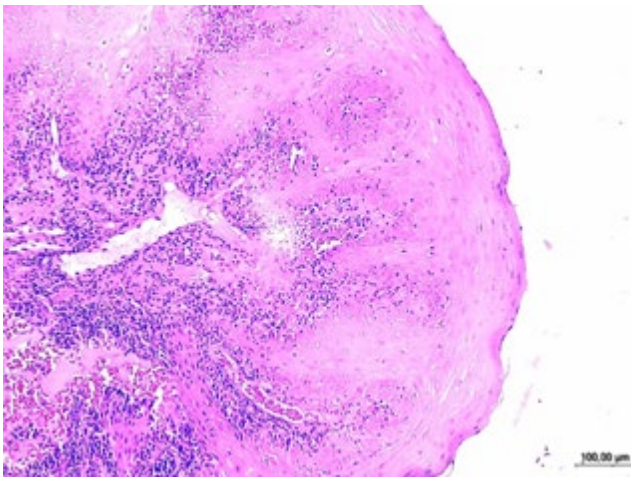


Figure 3. Angiomatosis, plethora and inflammatory infiltration.

ISSN 1996-353X
ISSN 2311-6951

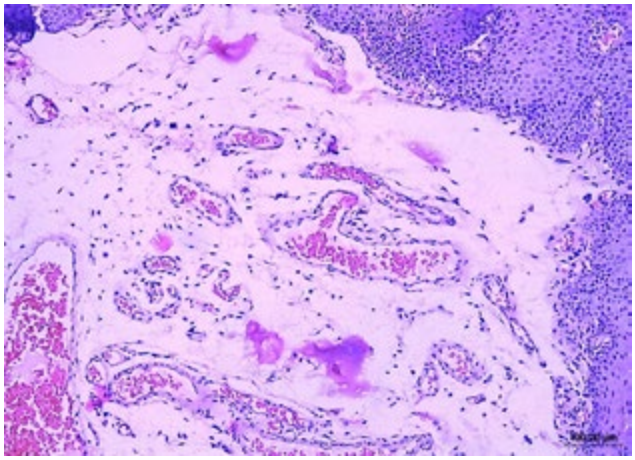


Figure 4. Angiomatosis and disorganization of subepithelial tissues.

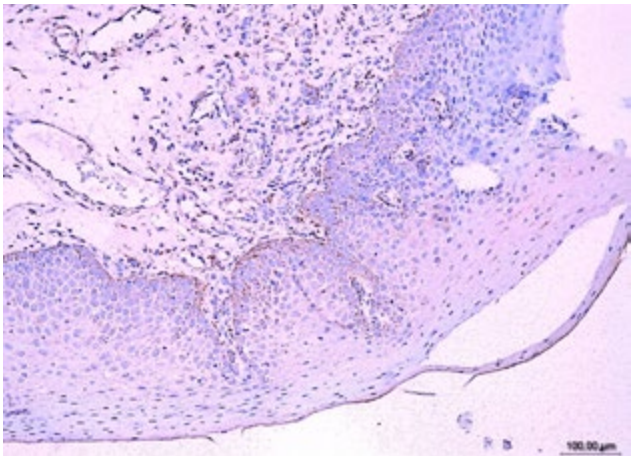


Figure 5. Positive HPV reaction in the squamous epithelium of oral mucosa.

in the basal layer of stratified squamous epithelium of oral mucosa and dispersed positive reaction in the dendritic cells of underlying connective tissue. HPV IHC stain, magnification x100.

Representative IHC p16 staining image showing diffuse cytoplasmic reaction in the layer of stratified squamous epithelium of oral mucosa. p16 IHC stain, magnification x200.

Box plot 1 illustrates the statistically significant difference in the distribution of number of vessels between study groups.

Box plot 2 illustrates the statistically significant difference in the distribution of number of intraepithelial lymphocytes between study groups.

Box plot 3 illustrates the statistically significant difference in the distribution of number of vessels between study groups.

Box plot 4 illustrates the statistically significant difference in the distribution of proliferation index (Ki-67) between study groups.

Discussion. Current research highlights the morphological changes of the soft palatine tissues in patients

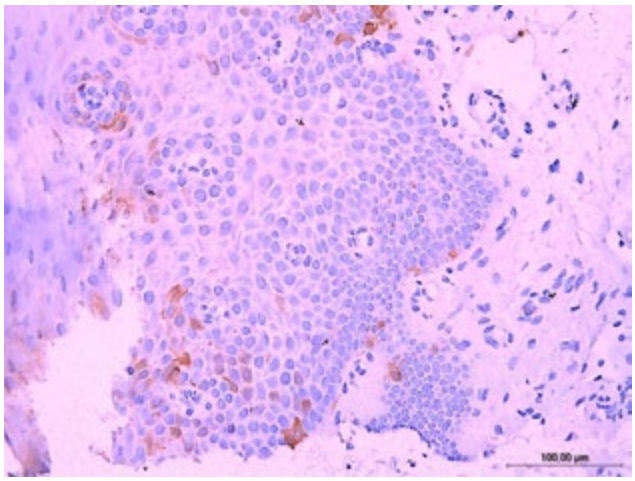


Figure 6. Positive p16-reaction in the squamous epithelium of oral mucosa.

with II stage obstructive sleep apnea syndrome. Despite statistically significant results and prominent histological picture there are several limitations in this research. Firstly, we did not take into account clinical indicators. Even more sample was homogeneous except of age of patients.

Second limitation is quite small size of samples. To obtain profound results it is recommended to expand such study and include patients with different stages of OSA syndrome with different concomitant conditions. Previously only one study was published regarding role of human papilloma virus in the development of OSA syndrome. Baldwin et al. tried to find out whether there are any differences in the BMI, apnea/hypopnea index, gender or age between patients with or without oral HPV-infection (Baldwin et al., 2017). They did not find any statistically significant differences. In our study we also did not concentrated on populational and clinical features of the sample due to its small size. Nevertheless, negative results in study conducted by Baldwin et al. could be connected to only few HPV-positive cases (6 from 99 studied). Accordingly, it sounds logically to repeat their research with groups being comparable in size.

Third and very important limitation is the isolated approach to the inflectional factor. Though human papilloma virus is key pathogen in the epithelial pathology spectrum of found changes wasn't linked only to epithelial layer. Moreover, oral microbiota is very heterogenous and includes several hundred to several thousand diverse species (Arweiler, & Netuschil, 2016). The disturbed balance of oral biofilms predispose person to many dental and systemic diseases; bacterial communities play a crucial role in the maintenance of physiological, metabolic and immunological functions (Kilian et al., 2016). Today there is a plot of evidence regarding changes of oral microbiome in the overweight and obese patients. At the same time these factors have strong correlation with the development of OSA (Jia et al., 2020), correspondingly it is important to study the cross-relation between changes in oral microbiome and development of upper airways

ISSN 1996-353X
ISSN 2311-6951

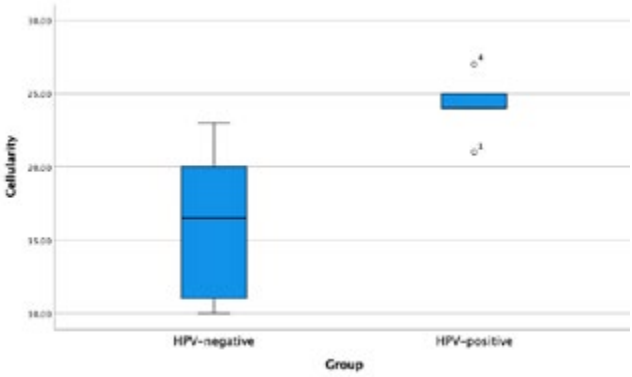
Table 2 shows the results of morphometric analysis among the groups.

Parameter	HPV-negative group	Coefficient of variation, %	HPV-positive group	Coefficient of variation, %
Number of cellular layers	16 (±4,78)	29,9	24,2 (±2,17)*	8,96
Number of intraepithelial lymphocytes (per 100 epitheliocytes)	3,3 (±1,77)	53,54	37,8 (±20,97)*	55,47
Number of vessels per x100 field	10,7 (±2,67)	24,94	21 (±8,46)*	40,27
p16-positivity	0	-	5	-
Ki-67 proliferation index	7,3 (±2,71)	37,12	17,6 (±2,51)*	14,26

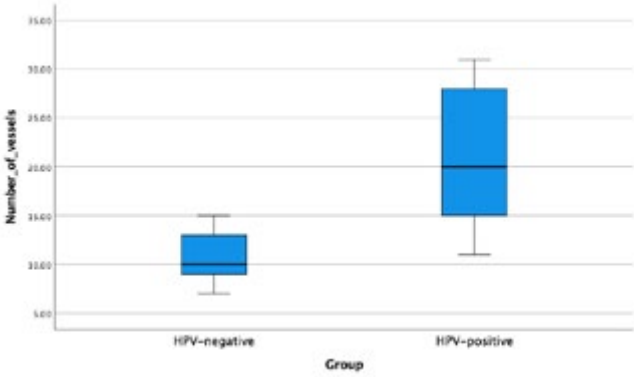
* - the presence of a statistically significant difference between indicators before and after surgery, p <0.05 (calculated using the Mann-Whitney test for unrelated samples).

obstruction. Some studies were conducted previously but the results are contradictory. For example, P. Jia and colleagues failed to find difference in the composition of the microbiota of salivary glands in patients with or without OSA syndrome (Jia et al., 2020). However, one study shows the presence of common respiratory viruses such as rhinovirus, adenovirus, human metapneumovirus, respiratory syncytial virus, and corona virus in children with obstructive sleep apnea (Yeshuroon-Koffler, Shemer-Avni, Keren-Naus, & Goldbart, 2015). Also, S. Mashaqi and D. Gozal published a research dedicated to the gut dysbiosis in the obstructive sleep apnea induced hypertension. Scientists stated that gut dysbiosis seems to be an important factor in the pathophysiology of OSA-induced hypertension (Mashaqi, & Gozal, 2019). Thereby, furthers studies of the microbiome changes and viral factors in the development of OSA seems to be relevant and promising and can bring new light in the understanding on this condition.

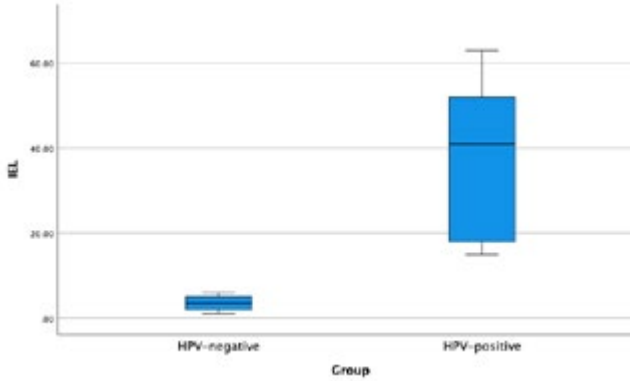
Conclusions. In patients with snoring and obstructive sleep apnea syndrome, hypertrophy of the soft palate structures is observed caused by changes in epithelial and connective tissue components. Subepithelial structures underdo the disorganization of connective tissue



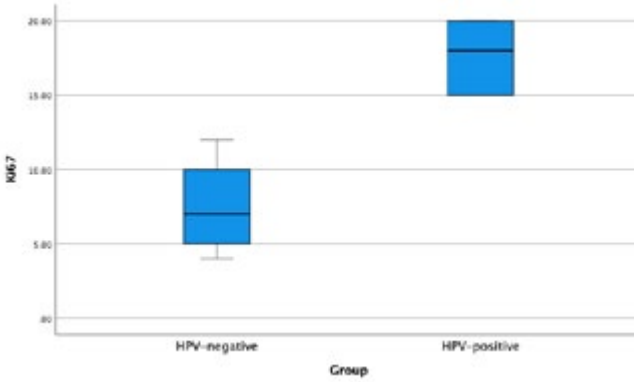
Box plot 1. Distribution of the number of vessels among the groups.



Box plot 2. Distribution of the number of intraepithelial lymphocytes among the groups.



Box plot 3. Distribution of the number of vessels among the groups.



Box plot 4. Distribution of proliferation index (Ki-67) among the groups.

ISSN 1996-353X
ISSN 2311-6951

components with a violation of the histoarchitectonics of collagen fibers, edema and angiomatosis. Thus, the study revealed a number of irreversible pathological processes of soft palate tissues, which is the basis for the choice of surgical treatment tactics including the resection of excess tissue.

At the same time HPV-infection leads to more pronounced changes in the epithelial layer and subepithelial tissue with concomitant inflammation that likely to create a negative background for further treatment of OSA syndrome.

Financing. This study did not receive funding.

Conflict of interest. None of the authors received research grants, speaker's fees from any companies and is not a member of commissions.

Authors contribution: concept, methodology, formal analysis - D.R., G.S.; research, resources, data curation, written - D.R., G.S., N.S., D.O.; original project preparation, review and editing, visualization, supervision, project administration, acquisition of financing - D.R., G.S., N.S., D.O., N.O.

Consent to publication. All authors have read and approved the final version of the manuscript. All authors have agreed to publish this manuscript.

LITERATURE

Spicuzza, L., Caruso, D., & Di Maria, G. (2015). Obstructive sleep apnoea syndrome and its management. *Therapeutic advances in chronic disease*, *6*(5), 273–285.

Mannarino, M. R., Di Filippo, F., & Pirro, M. (2012). Obstructive sleep apnea syndrome. *European journal of internal medicine*, *23*(7), 586–593.

Denysenko R, Dikhtiaruk O, Naumenko O. (2020). Influence of modified uvulopalatopharyngoplasty on body weight and quality of night sleep in patients with low compliance to cpap therapy.

Lévy, P., Kohler, M., McNicholas, W. T., Barbé, F., McEvoy, R. D., Somers, V. K., Lavie, L., & Pépin, J. L. (2015). Obstructive sleep apnoea syndrome. *Nature reviews. Disease primers*, *1*, 15015.

Marin, J. M., Carrizo, S. J., Vicente, E., & Agusti, A. G. (2005). Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. *Lancet (London, England)*, *365*(9464), 1046–1053.

Sutherland, K., Phillips, C. L., & Cistulli, P. A. (2015). Efficacy versus effectiveness in the treatment of obstructive sleep apnea: CPAP and oral appliances. *J Dent Sleep Med*, *2*(4), 175-181.

Pépin, J. L., Leger, P., Veale, D., Langevin, B., Robert, D., & Lévy, P. (1995). Side effects of nasal continuous positive airway pressure in sleep apnea syndrome. Study of 193 patients in two French sleep centers. *Chest*, *107*(2), 375–381.

Mysliwiec, V., Martin, J. L., Ulmer, C. S., Chowdhuri, S., Brock, M. S., Spevak, C., & Sall, J. (2020). The Management of Chronic Insomnia Disorder and Obstructive Sleep Apnea: Synopsis of the 2019 U.S. Department of Veterans Affairs and U.S. Department of Defense Clinical Practice Guidelines. *Annals of internal medicine*, *172*(5), 325–336.

Friberg, D., Ansved, T., Borg, K., Carlsson-Nordlander, B., Larsson, H., & Svanborg, E. (1998). Histological indications of a progressive snorers disease in an upper airway muscle. *American journal of respiratory and critical care medicine*, *157*(2), 586–593.

Liu, Y., Gao, L., Lv, W., Lin, L., Wang, Y., He, H., Jiang, F., & Feng, F. (2019). Histological, Ultrastructural, and Physiological Evaluation of a Rat Model of Obstructive Sleep Apnea Syndrome. *Medical science monitor : international medical journal of experimental and clinical research*, *25*, 1806–1813.

Gillison, M. L., Broutian, T., Pickard, R. K., Tong, Z. Y., Xiao, W., Kahle, L., Graubard, B. I., & Chaturvedi, A. K. (2012). Prevalence of oral HPV infection in the United States, 2009-2010. *JAMA*, *307*(7), 693–703.

Du, J., Nordfors, C., Ährlund-Richter, A., Sobkowiak, M., Romanitan, M., Näsman, A., ... & Dalianis, T. (2012). Prevalence of oral human papillomavirus infection among youth, Sweden. *Emerging infectious diseases*, *18*(9), 1468.

Feller, L., Khammissa, R. A., Wood, N. H., & Lemmer, J. (2009). Epithelial maturation and molecular biology of oral HPV. *Infectious agents and cancer*, *4*, 16.

Baldwin, B. J., Chitale, D., Chen, K. M., Worsham, M. J., & Yaremchuk, K. (2017). Investigation into the presence of human papillomavirus in patients with obstructive sleep apnea. *The Laryngoscope*, *127*(5), 1231–1234.

Boudewyns, A., Marklund, M., & Hochban, W. (2007). Alternatives for OSAHS treatment: selection of patients for upper airway surgery and oral appliances. *European Respiratory Review*, *16*(106), 132-145.

Arweiler, N. B., & Netuschil, L. (2016). The oral microbiota. *Microbiota of the Human Body*, 45-60.

Kilian, M., Chapple, I. L., Hannig, M., Marsh, P. D., Meuric, V., Pedersen, A. M., Tonetti, M. S., Wade, W. G., & Zaura, E. (2016). The oral microbiome - an update for oral healthcare professionals. *British dental journal*, *221*(10), 657–666.

Jia, P., Zou, J., Yin, S., Chen, F., Yi, H., & Zhang, Q. (2020). Analysis of the Salivary Microbiome in Obstructive Sleep Apnea Syndrome Patients. *The Canadian journal of infectious diseases & medical microbiology = Journal canadien des maladies infectieuses et de la microbiologie medicale*, *2020*, 6682020.

Yeshuroon-Koffler, K., Shemer-Avni, Y., Keren-Naus, A., & Goldbart, A. D. (2015). Detection of common respiratory viruses in tonsillar tissue of children with obstructive sleep apnea. *Pediatric pulmonology*, *50*(2), 187–195.

Mashaqi, S., & Gozal, D. (2019). Obstructive Sleep Apnea and Systemic Hypertension: Gut Dysbiosis as the Mediator?. Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine, 15(10), 1517–1527.

Ukrainian Scientific Medical Youth Journal
Issue 4 (127), 2021
ISSN 1996-353X
ISSN 2311-6951

МОРФОЛОГІЧНІ ЗМІНИ В ТКАНИНАХ М'ЯКОГО ПІДНЕБІННЯ, ЩО СТОЯТЬ ЗА СИНДРОМОМ ОБСТРУКТИВНОГО АПНОЕ СНУ: ЗАГАЛЬНА КАРТИНА ТА РОЛЬ ВІРУСУ ПАПІЛОМИ ЛЮДИНИ.

Денисенко Роман[1], Гичка Сергій[2], Ніколаенко Софія [2], Діхтярук Олександр[1], Науменко Олександр[1]

[1] Кафедра оториноларингології, Національний медичний університет ім. Богомольця, Київ, Україна

[2] Кафедра патологічної анатомії, Національний медичний університет ім. Богомольця, Київ, Україна

Анотація: хропіння та синдром обструктивного апное сну (СОАС) є серйозною медичною проблемою, оскільки призводять до комплексу ускладнень з боку різних систем організму, порушують соціально-економічну сферу та стигматизують пацієнтів. На сьогоднішній день розроблено комплекс методів лікування, найефективнішими з яких є консервативна терапія з використанням CPAP та оперативні втручання – різні модифікації увулопалатофарингопластики. Однак лише невелика кількість досліджень з'ясувала патологію тканин м'якого піднебіння у пацієнтів із хронічним захворюванням та СОАС. Розуміння морфологічних змін є одним із ключових аспектів розробки лікувальної тактики. Метою поточного дослідження є обґрунтування вибору хірургічного втручання при лікуванні хропіння та СОАС шляхом опису морфологічних змін м'якого піднебіння та оцінки впливу ВПЛ-інфекції на прогресування ремоделювання м'якого піднебіння. Дослідження включало зразки м'яких тканин піднебіння, які були вилучені під час операції з приводу хропіння та СОАС у 15 пацієнтів. Гістологічні (H&E) та імуногістохімічні методи (Ki-67, p16, вірус папіломи людини). Усі пацієнти були розділені на дві групи відповідно до ВПЛ-позитивності: 5 осіб у ВПЛ-позитивній групі та 10 осіб у ВПЛ-негативній групі. Для показників оцінювали: кількість клітинних шарів (CL), кількість внутрішньоепітеліальних лімфоцитів (на 100 епітеліоцитів) (IEL), кількість судин на x100 поле (NV), індекс проліферації Ki-67 (PI). Результати в групі ВПЛ+: CL - 24,2 (±2,17); IEL - 37,8 (±20,97), NV - 21 (±8,46); ПІ - 17,6 (±2,51). У групі ВПЛ: CL - 6 (±4,78); IEL - 3,3 (±1,77); НВ - 10,7 (±2,67); ПІ - 7,3 (±2,71). Критерій Манна-Уітні показує статистично значущу різницю між групами за всіма зазначеними показниками. Підсумок: у пацієнтів із хропінням та синдромом обструктивного апное сну відзначалася гіпертрофія структур м'якого піднебіння, спричинена зміною компонентів епітелію та сполучної тканини. Підепітеліальні структури

МОРФОЛОГИЧЕСКИЕ ИЗМЕНЕНИЯ В ТКАНЯХ МЯГКОГО НЕБА, СТОЯЩИЕ ЗА СИНДРОМОМ ОБСТРУКТИВНОГО АПНОЭ СНА: ОБЩАЯ КАРТИНА И РОЛЬ ВИРУСА ПАПИЛЛОМЫ ЧЕЛОВЕКА.

Денисенко Роман[1], Гичка Сергей[2], Николаенко София [2], Дихтярук Александр[1], Науменко Александр[1]

[1] Кафедра оториноларингологии, Национальный медицинский университет им. Богомольца, Киев, Украина

[2] Кафедра патологической анатомии, Национальный медицинский университет им. Богомольца, Киев, Украина

Аннотация: храп и синдром обструктивного апноэ сна (СОАС) являются серьезной медицинской проблемой, поскольку приводят к комплексу осложнений со стороны разных систем организма, нарушают социально-экономическую сферу и стигматизируют пациентов. На сегодняшний день разработан комплекс методов лечения, наиболее эффективными из которых являются консервативная терапия с использованием CPAP и оперативные вмешательства – различные модификации в улопалатофарингопластике. Однако лишь небольшое количество исследований выяснило патологию тканей мягкого неба у пациентов с хроническим заболеванием и СОАС. Но понимание морфологических изменений является одним из ключевых аспектов разработки лечебной тактики. Целью текущего исследования является обоснование выбора хирургического вмешательства при лечении храпа и СОАС путем описания морфологических изменений мягкого неба и оценки влияния ВПЧ-инфекции на прогрессирование ремоделирования мягкого неба. Исследование включало в себя образцы мягких тканей неба, которые были изъяты во время операции по храпу и СОАС у 15 пациентов. Гистологические (H&E) и иммуногистохимические методы (Ki-67, p16, вирус папилломы человека). Все пациенты были разделены на две группы согласно ВПЧ-положительности: 5 человек в ВПЧ-положительной группе и 10 человек в ВПЧ-отрицательной группе. Для показателей оценивали количество клеточных слоев (CL), количество внутриэпителиальных лимфоцитов (на 100 эпителиоцитов) (IEL), количество сосудов на x100 поле (NV), индекс пролиферации Ki-67 (PI). Результаты в группе ВПЧ+: CL – 24,2 (±2,17); IEL – 37,8 (±20,97), NV – 21 (±8,46); ПИ – 17,6 (±2,51). В группе ВПЧ: CL – 6 (±4,78); IEL – 3,3 (±1,77); НВ – 10,7 (±2,67); ПИ – 7,3 (±2,71). Критерий Манна-Уитни показывает статистически значимую разницу между группами по всем указанным показателям. Итог: у пациентов с храпом и синдромом обструктивного

ISSN 1996-353X
ISSN 2311-6951

підтримують дезорганізацію компонентів сполучної тканини з порушенням гістоархітектоніки колагенових волокон, набряком і ангіоматозом. Таким чином, в ході дослідження виявлено ряд незворотних патологічних процесів тканин м'якого піднебіння, що є основою для вибору тактики хірургічного лікування, в тому числі з резекції надлишкової тканини. У той же час ВПЛ-інфекція призводить до більш виражених змін епітеліального шару та субепітеліальної тканини з супутнім запаленням, що може створити негативний фон для подальшого лікування синдрому СОАС.

Ключові слова: синдром обструктивного апное сну, гістологічні зміни, ВПЛ-інфекція, хірургічне втручання при ОАС.

апноэ сна отмечалась гипертрофия структур мягкого неба, вызванная изменением компонентов эпителия и соединительной ткани. Подэпителиальные структуры поддерживают дезорганизацию компонентов соединительной ткани с нарушением гистоархитектоники коллагеновых волокон, отеком и ангиоматозом. Таким образом, в ходе исследования обнаружен ряд необратимых патологических процессов тканей мягкого неба, являющихся основой для выбора тактики хирургического лечения, в том числе из резекции избыточной ткани. В то же время ВПЧ-инфекция приводит к более выраженным изменениям эпителиального слоя и субэпителиальной ткани с сопутствующим воспалением, что может создать отрицательный фон для дальнейшего лечения синдрома СОАС.

Ключевые слова: синдром обструктивного апноэ сна, гистологические изменения, ВПЧ-инфекция, хирургическое вмешательство при ОАС.