Original Article

Gender-Wise Histological Differences in the Human Upper Lip

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Abstract

Introduction: Knowledge of morphometry of lip lining help in deciding the best site for choosing graft for its better uptake during several dermal grafting procedures following craniofacial cancers or cosmetic procedures. It also proves useful in dermatopharmacokinetics, in which we monitor the effect of drugs acting on connective tissue by translabial route and lip augmentation surgeries (esthetic surgery) where care is to be given for dermal fillers not to be injected into the muscle core of lip. **Materials and Methods:** Ten human male cadavers and 10 human female cadavers were procured. The rectangle-shaped skin specimen (1 cm × 1 cm) through the upper lip was stained with hematoxylin and eosin stain. A total of 40 slides were prepared. Readings were obtained with the help of CATCAM E series HD cameras which was installed in light microscope. **Results:** The mean value of thickness of skin (epidermis + dermis) of the lip was 664.72 μm among males while 769.20 μm among females. **Conclusion:** The epithelium of females is marginally thicker than males. Edp: sc (epidermis/stratum corneum) ratio can suggest that giving drugs through translabial route will be easy in females as compared to males in the upper lip as the stratum corneum is the main barrier in drug transfusion and its absorption secondary to epidermis as a whole. The number of rete pegs per field at the dermoepidermal junction was higher in males which ensures more stability of skin of male lips compared to females.

Keywords: Dermatopharmacokinetics, mucocutaneous junction, rete pegs, vermillion

Introduction

Knowledge of basic elements provides opportunity to make a clear vision of the structure of any organ. Researches emphasized that epidermis and its components are irregular undulating structures. Their depth is an important determinant of percutaneous absorption of ultraviolet rays as stratum corneum acts as rate-limiting barrier to it. Therefore epidermal thickness values help in evaluating, ultraviolet radiation-induced carcinogenesis and aging.[1] The knowledge of morphometry of various components of the skin of lip may be helpful to make an approach for induction and transfusion of drugs by normalizing drug penetration profiles through the translabial route during dermatopharmacokinetic studies.[2] As stratum corneum is the principal barrier to drug absorption too.[3] Dermatosurgery and esthetics surgery deals with surgical aspects of the skin and its appendages. Knowledge of the physical architecture of lip is of great importance in dermal grafting as well where the success of grafting depends on matching skin from donor and recipient sites.[4] In today's world with the evolution of microsurgical technique, several dermal grafting procedures are done at lip to restore tissue loss following trauma or tumor excision following craniofacial cancers or cosmetic procedures[5] Lips are fleshy folds lined externally by the skin and internally by mucus membrane and it bounds the oral fissure. The upper and lower lips are referred to as the "labium superius oris" and "labium inferius oris," respectively.[6] A mucocutaneous junction is defined as a transition zone where the oral and skin epithelial surfaces meet, for example, the lip contains the vermilion, which is a transitional zone between the stratified squamous epithelia of the skin and oral mucosa.[7] The mucocutaneous junction, for example, the eyelid and lip are the focal point of mucosal epithelial cell differentiation activities and employ similar cellular mechanisms[8] which is the basis for many reconstructional surgeries, for example,

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eyelid reconstruction by skin, mucocutaneous junction, mucosa, and muscle of lip.[9]

Skin is made up of two layers, namely epidermis and dermis with a basement membrane zone in between and a buttress of subcutaneous fat underneath.[10]

Aging and sex particularly affect lips with changes in thickness and vermillion dimensions.[11] The sex steroids are intricately involved in supporting the structure of skin and its function. The interplay of growth factors and sex steroids affects sebum productions; androgen and estrogens local synthesis and their receptor-mediated action affect sweat gland and hair follicle. Hence with advancing age altered balance of abovementioned hormones and their expression enzymes and receptors within the skin itself influence salient gender differences in aging skin.[12]

Increase in skin thickness is a characteristic aspect of chronoaging of facial skin.[13] Collagen density in skin is less in females as compared to males probably due to androgen since it is increased in patients with primary cutaneous virilism. It increases with age in both sexes up to 30–40 years after which it starts decreasing. On the other hand, elastic fiber density increases in both sexes in the first decade of life followed by drop particularly marked in males. After 20 years of age, relative volume of elastic fibers displays a decreasing trend in females in contrast to males where it attains the highest values beyond 40s.[14]

Materials and Methods

The present observational study was carried out in the Department of Anatomy in collaboration with the Department of Forensic Medicine and Toxicology, King George's Medical University, Lucknow, Uttar Pradesh, from September 2018 to August 2019. Ethical clearance was obtained from the Institutional Ethics Committee, King George's Medical University, Lucknow, through letter no. (1124/Ethics/18).

For the present study, 10 human male cadavers and 10 female cadavers were procured with the size dimension of 1 cm × 1 cm. Out of 20 samples of lip, 12 samples were taken from fresh male donated body received in the department of anatomy 4 to 5 h after death, and the rest eight samples were collected from forensic medicine 5 to 6 h after death. The age of male cadavers ranged between 5 and 75 years (mean age 45.5 years) while of female it ranged between 60 and 70 years (mean age 67 years).

The cutaneous area present with abrasions, breech, and infections such as boils, crusting, blackening of the skin, and hemorrhaged sites were not taken for study. Care was taken for the specimen, not to have any kind of image artifacts from movement or orthodontic material. The rectangle-shaped skin specimen measuring 1 cm × 1 cm was taken through the upper lip of each participants which included its vermillion region.

Hence, a total of 20 samples were taken. For each lip sample, two slides were prepared and stained with hematoxylin and eosin. Each parameter was determined per slide and then averaged to one data set to avoid the chance of error. Each of the slide contained horizontal sections of tissue. Parameters such as epithelium thickness, depth, number, and pattern of rete pegs at the dermoepidermal junction, Thickness of dermis were taken in ×10 except thickness of stratum corneum (Tsc), number of layers of stratum granulosum and spinosum which were observed in ×40. The abovementioned parameters were measured with the help of CATCAM E series HD cameras which was installed in light microscope after removing the eyepiece as relay lens is built into the camera itself. Catymage software was installed in my personal laptop and scales were calibrated at ×4, ×10, ×40, and ×100. Camera was connected to a USB 2.0 port on my laptop. USB 2.0 high-quality images were captured. Every slide was read carefully, and various parameters (thickness) were measured using scale. The value of each parameter in micrometer was entered into Word Excel sheet. The mean value of each parameter was entered into tabulated form. The 21st version of SPSS software (IBM corporation Business Analytical Software, Chicago, Illinois, USA) was used to analyze statistical changes. The microphotography was done with the help of device incorporated within the software. The device was installed in a laptop and connected with microscope and the photograph was clicked which was focused on the screen.

Results

The mean value of thickness of skin (epidermis + dermis) of lip was 664.72 μm among males while 769.20 μm among females. On comparing the vermillion region of the upper lip of males and females, females as compared to males had a higher number of layers of stratum spinosum, papillary dermis, and total skin thickness, the rest of the above parameters were found to be higher in males as compared to females.

Statistically significant differences among male and female were observed only for thickness of epidermis, Edp: Sc ratio, number of layers of stratum spinosum, number of rete pegs/field, and papillary dermis.

Discussion

Histologic analysis of the topographical variations of normal skin of lip is of relevance in dermatological research. The lip region of the face is of utmost significant value in the looks of an individual. The skin of lip consists of two distinct layers, epidermis and dermis. Each component varies according to age, gender, race, and anatomic location.[15]

The thickness of skin of lip:

The total thickness of lip skin (epidermis and dermis) was found to be higher in females as compared to males [Figure 1]. Takema Y *et al*. studied the skin thickness of 170 Japanese females using 20 MHz A mode Usg scanner at the corner of

Table 1: Gender-wise comparison of different parameters at upper lip in the vermillion region

Parameter (μm)	Males				Females				Student *t*-test	
	n	Minimum	Maximum	Mean±SD	*n*	Minimum	Maximum	Mean±SD	*t*	*P*
Thickness of Edp	10	43.00	136.00	86.72±31.49	10	165.00	248.00	194.40±33.23	−6.136	<0.001
Thickness of Sc	10	7.69	19.80	14.21±4.69	10	11.56	13.00	12.46±0.65	0.813	0.431
Edp:Sc ratio	10	3.58	15.28	7.28±4.94	10	12.82	21.45	15.74±3.56	−3.385	0.005
Number of layers of stratum spinosum	10	3.00	7.00	4.70±1.16	10	8.00	10.00	9.00±0.71	−7.538	<0.001
Number of layers of stratum granulosum	10	1.00	3.00	2.20±0.79	10	2.00	3.00	2.40±0.55	−0.505	0.622
Number of rete pegs/field	10	6.00	8.00	7.10±0.88	10	5.00	7.00	5.80±1.10	2.502	0.026
Depth of rete pegs	10	109.00	468.00	225.60±126.32	10	203.00	335.00	256.60±51.34	−0.520	0.612
Pd	10	39.00	111.00	63.50±20.12	10	167.00	201.00	186.40±14.12	−12.14	<0.001
Rd	10	152.00	879.00	514.50±301.21	10	355.00	402.00	388.40±19.73	0.918	0.375
Total dermis (Pd+Rd)	10	204.00	919.00	578.00±296.76	10	533.00	596.00	574.80±25.61	0.024	0.982
Total skin thickness	10	272	1012.98	664.72±293.11	10	698	835	769.2±52.6	−0.777	0.451

Edp: Epidermis, Sc: Stratum corneum, Pd: Papillary dermis, Rd: Reticular dermis, SD: Standard deviation

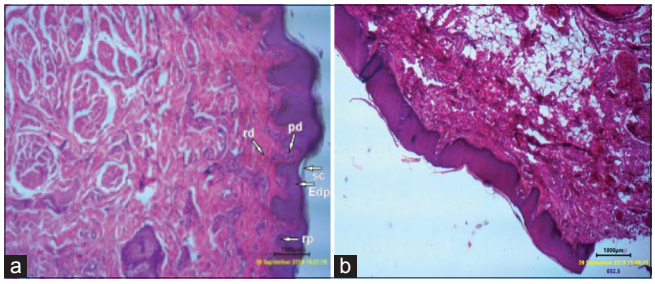

Figure 1: (a) Microphotograph of the vermillion region of male lip at ×4 of the upper lip in males showing Edp (epidermis), pd (papillary dermis), rd (reticular dermis) sc, 9 stratum corneum, rp (rete pegs) (b) Microphotograph of the vermillion region of female upper lip at ×4

mouth as 1.62 ± 0.19 mm which is not found to be in unison with our study findings.[16] Our findings were relatively less [Table 1]. Probably different ethnicity and site of lip of female subject and mode of measurement might be responsible. Ha Richard *et al.* observed the thickness of skin of the upper lip vermillion in three north American individuals as 0.79 ± 0.16 mm in male subject (age 78 years), 0.68 ± 0.09 mm in the second male subject (age 82 years), and 1.01 ± 0.01 mm in female subject (51-year-old).[17] In our study, we found total skin values of males found to be in consensus with above data, however, females' values were less [Table 1]. The reason for this mismatch can be accounted as different age groups, sample size, and ethnicity of female subjects in both the studies. Chopra *et al*. observed total skin thickness of the upper lip vermillion in three males and seven females cadavers (81.6 ± 11.3 years) of American origin using the triplicate computerized method as 1496.12 ± 57.79 μm.[18] In our study, the mean total skin thickness at vermillion in males was 664.72 ± 293.11 μm and in females was 769.2 ± 52.6 μm. Our study findings were relatively less [Table 1].

Thickness of epidermis

Depth of epithelium was more in females as compared to males [Figure 1]. The upper lip of males exhibited statistically significant difference in comparison to females. Jacobi *et al.* in a histological study of lip epithelium of German subjects described its depth to be 74–148 μm. They did not mention the gender, age, or even site of lip.[19] Despite this, our male observations were coinciding with their values [Table 1]. Madhav *et al*. reported in their review article, the mean epithelial thickness of skin, vermillion, and oral mucosa as 46 μm, 97 μm, and 218 μm, respectively.[20] Our study findings of the vermillion region of males' upper lip are in consensus with above measurements despite the fact that the article remain silent for age, gender, site, or even ethnicity.

Chopra *et al*. observed epidermal thickness of the upper lip vermillion in three male and seven female cadavers (81.6 ± 11.3 years) of American origin using triplicate computerized method as 62.62 ± 57.79 μm.[18] In our study, the mean epidermal thickness at vermillion in males was 86.72 ± 31.49 μm and in females was 194.40 ± 33.23 μm, respectively [Table 1]. Although the depth of epidermis was coinciding with our values of male subjects but our values of females were relatively higher as compared to above study. The differences in observations can be clearly explained by the fact that in these study measurements from both genders were averaged.

Thickness of stratum corneum

Similarly, epidermis and stratum corneum also exhibited remarkable gender difference at the upper lip. The depth of stratum corneum was found to be more in males as compared to females [Figure 1]. Jacobi *et al*. in their light microscopic study observed the Tsc of lip in eight human subjects native of Germany, as 13–28 μm thick.[19] In our study, values of stratum corneum thickness of both genders approximate to above range [Table 1].

Edp: Sc ratio

Edp: Sc ratio also exhibited gender differences at lip. The study of ratio depicted that contribution of the stratum

corneum in thickness of epidermis was less among females as compared to males. As stratum corneum act as a protection against frictional forces, is assumed to be thicker at places where such forces are relatively more. This hypothesis was proved right in our study. Because, in males, the Tsc was more than in females at upper lip, an area of mustache which is repeatedly shaved, hence subjected to greater frictional forces.

Number of cell layers of stratum spinosum and stratum granulosum

In the present study, the number of cell layers of stratum spinosum was higher in females [Figure 1] as compared to males corresponding to Edp. It ranged from 4 to 13 in number. No characteristic gender-specific pattern was observed. No comparison could be done as literature remain silent for these parameters.

Rete pegs: Number and depth

The number of rete pegs per field showed a remarkable gender-specific differences. They were found more in males than in females [Figure 1 and Table 1]. The number and depth of rete pegs ensure stronger adherence between dermis and epidermis. Greater number of rete pegs ensures increase in number of basal germinative cells and greater surface area for superficial dermal capillary plexus for exchange of nutrients. The depth of rete peg was positively correlated with layers of stratum spinosum, stratum granulosum, and depth of stratum corneum. Jacobi *et al*. observed the thickness of rete ridges of lip in eight human natives of Germany using light microscope, approximately 150–300 μm thick which were found to be in consensus with the values in the vermillion region of lip in both genders [Table 1].[19] Comparison cannot be justified as the site of lip and sex of subjects are not mentioned in the article.

Dermis: Papillary, reticular, and total

Papillary dermis was found more in females as compared to males [Figure 1]. On the other hand, reticular dermis was found more in males as compared to females. Subsequently, total dermis was observed to be more in males than in females in the upper lip. In the microscopic study of Dimond and Montagna on four male subjects (aged 20, 22, 25, and 65 years) and one female subject (aged 30 years) found dermis of vermillion border to be 0.5 mm thick.[21] Data were found to be approximated to the findings at the upper lip in both genders [Table 1 and Figure 1].

Conclusion

The present observational study was undertaken to assess the gender-specific differences in lip histology at the upper lip. The mean value of epithelium of females is marginally thicker than males. The study of ratio depicted that contribution of the stratum corneum in thickness of epidermis was less among females as compared to males. Edp: sc ratio can also suggest that giving drug through the translabial route will be easy in females as compared to males in upper lip as stratum corneum is the main barrier in drug transfusion and its absorption secondary to epidermis as a whole. The number of rete pegs per field was higher in males as compared to females.

This study tried to create a baseline comparison to establish the presence of gender variation in lip morphometry which can set a standard to compare pathological and chronological changes. The measurement of skin thickness, stratum corneum, dermal thickness can also prove useful in esthetic surgery (lip augmentation surgery) as it is suggested that dermal fillers used in these surgeries should not be injected so deep because if it enters the muscle core of lip, it can cause granuloma or necrosis due to being highly viscous in nature.[22]

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Conflicts of interest

There are no conflicts of interest.

References

1. Robertson K, Rees JL. Variation in epidermal morphology in human skin at different body sites as measured by reflectance confocal microscopy. Acta Derm Venereol 2010;90:368-73.
2. Saxena S, Pankaj AK, Panwar S, Rani A, Chopra J, Rani A. Histological changes at the commissure of the lip on approaching from its cutaneous to the mucosa region in males. Natl J Maxillofac Surg 2021;12:88-92.
3. Alberti I, Kalia YN, Naik A, Guy RH. Assessment and prediction of the cutaneous bioavailability of topical terbinafine, *in vivo*, in man. Pharm Res 2001;18:1472-5.
4. Whitton JT, Everall JD. The thickness of the epidermis. Br J Dermatol 1973;89:467-76.
5. Kinikoglu B, Damour O, Hasirci V. Tissue engineering of oral mucosa: A shared concept with skin. J Artif Organs 2015;18:8-19.
6. Krishnapriya KR, Vishnu S, Sreeja CN. Translabial route: As a platform for systemic drug delivery. J Chem Pharm Res 2015;7:335-48.
7. Bayar GR, Kuo S, Marcelo CL, Feinberg SE. *In vitro* development of a mucocutaneous junction for lip reconstruction. J Oral Maxillofac Surg 2016;74:2317-26.
8. Riau AK, Barathi VA, Beuerman RW. Mucocutaneous junction of eyelid and lip: A study of the transition zone using epithelial cell markers. Curr Eye Res 2008;33:912-22.
9. Whittaker CJ, Wilkie DA, Simpson DJ, Deykin A, Smith JS, Robinson CL. Lip commissure to eyelid transposition for repair of feline eyelid agenesis. Vet Ophthalmol 2010;13:173-8.
10. Venkataram M. Textbook on Cutaneous and Aesthetic Sugery. Vol. 1. New Delhi, India: Jaypee Brothers Medical Publishers Pvt. Ltd.; 2012. p. 4-5.
11. Sental Kumar B, Paneer Selvi G. Sex determination by morpometry of lips. J Krisna Inst Med Sci Univ 2018;7:42-8.
12. Farage MA, Miller KW, Elsner P, Maibach HI. Structural characteristics of the aging skin: A review. Cutan Ocul Toxicol 2007;26:343-57.
13. Shuster S, Black MM, McVitie E. The influence of age and sex on skin thickness, skin collagen and density. Br J Dermatol 1975;93:639-43.
14. Vitellaro-Zuccarello L, Cappelletti S, Dal Pozzo Rossi V, Sari-Gorla M. Stereological analysis of collagen and elastic fibers in the normal human dermis: Variability with age, sex, and body region. Anat Rec 1994;238:153-62.
15. Wickett RR, Visscher MO. Structure and function of epidermal barrier. Am J Infect Control 2006;34:98-110.

16. Takema Y, Yorimoto Y, Kawai M, Imokawa G. Age -related changes in the elastic properties and thickness of human facial skin. British journal of Dermatology 1994;131:641-8.
17. Ha RY, Nojima K, Adams WP Jr., Brown SA. Analysis of facial skin thickness: Defining the relative thickness index. Plast Reconstr Surg 2005;115:1769-73.
18. Chopra K, Calva D, Sosin M, Tadisina KK, Banda A, De La Cruz C, *et al.* A comprehensive examination of topographic thickness of skin in the human face. Aesthet Surg J 2015;35:1007-13.
19. Jacobi U, Toll R, Audring H, Sterry W, Lademann J. The porcine snout – An *in vitro* model for human lips? Exp Dermatol 2005;14:96-102.
20. Madhav S, Yadav AP. Lip: An impressive and idealistic platform for drug delivery. J Pharm Res 2011;4:1060-2.
21. Dimond RL, Montagna W. Histology and cytochemistry of human skin. XXXVI. The nose and lips. Arch Dermatol 1976;112:1235-44.
22. Sánchez-Carpintero I, Candelas D, Ruiz-Rodríguez R. Dermal fillers: Types, indications, and complications. Actas Dermosifiliogr 2010;101:381-93.