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## Modifications and evaluation of smell and taste functions in total laryngectomy: systematic review

### *Alterações e avaliação das funções do olfato e do paladar em laringectomizados totais: revisão sistemática*

### ABSTRACT

The aim of this study was to systematically review the alterations in smell and taste functions in individuals who underwent total laryngectomy, as well as to identify in the literature some aspects involved in the evaluation of these functions in this population. We performed a systematic review on the databases Medline, LILACS and SciELO, and this data search occurred in October/2010. The search used keywords and free terms, and retrieved 84 articles, 79 from Medline, via Pubmed, and five from LILACS and SciELO. Sixteen of these articles were selected. Most studies in this review attested decline in sensory of smell and taste functions in individuals who underwent total laryngectomy and, although there is consensus regarding the damage caused to these functions by the nasal airflow interruption, it is not yet possible to evidence details in the mechanisms and structures involved, especially regarding the modifications in the olfactory mucous.

### RESUMO

O objetivo desse estudo foi rever de forma sistemática as alterações nas funções do olfato e do paladar em indivíduos submetidos à laringectomia total, bem como identificar na literatura os aspectos envolvidos na avaliação dessas funções nesta população. Foi realizada uma revisão sistemática a partir das bases de dados MedLine, LILACS e SciELO, tendo a busca de dados ocorrida em outubro/2010. Foram encontrados 84 artigos a partir da busca de descritores e termo livre, sendo 79 da Medline, via Pubmed, e cinco da LILACS e da SciELO. Destes, foram selecionados 16 artigos. A maioria dos estudos, nesta revisão, atestou diminuição das funções sensoriais do olfato e do paladar em indivíduos submetidos à laringectomia total e, embora haja consenso com relação aos prejuízos causados a essas funções pela interrupção do fluxo aéreo nasal, ainda não é possível evidenciar minuciosamente os mecanismos e estruturas envolvidas, principalmente no que se refere às alterações da mucosa olfatória.

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## INTRODUCTION

The sense of smell is the result of contact by air odor molecules with the receptors located in the nasal mucous<sup>(1)</sup>. Perceiving chemicals substances in the oral and nasal cavity, the olfactory and taste systems work together<sup>(2)</sup>, being the taste or gustatory sense a sensorchemics primary mechanism that defines, in association to other senses, the food intake<sup>(3)</sup>.

In the event of total laryngectomy as a surgical treatment of larynx cancer, there is removal of structures that produce the laryngeal sound and neighbors muscles, with the transfer of the nasal airflow definitely to the tracheostoma<sup>(4)</sup>, reflecting the commitment the odor molecules arrival to the olfactory epithelium by nasal inhalation, which causes changes in perception of smell and taste<sup>(5-8)</sup>.

The understanding of the gustatory and olfactory sense behavior in patients who underwent total laryngectomy may contribute to the clinical practice of health professionals and especially the speech therapist, who historically have worked with these individuals. The gain with the acquisition of such knowledge may directly influence the rehabilitation process of chewing and swallowing functions, these functions are closely related to smell and taste.

## OBJECTIVES

Given that a few studies that broach these issue, this study aims to systematically review the changes in the smell and taste functions in individuals who underwent total laryngectomy, as well as to identify in the literature the aspects involved in the evaluation of these functions in those population.

## RESEARCH STRATEGY

The systematic literature review was performed from the data bases Medical Literature Analysis and Retrieval System Online (Medline), Latin American and Caribbean Health Sciences Literature (LILACS) and Scientific Electronic Library Online (SciELO), and the research data occurred in october/2010. For each one, it was used a strategy specific to the intersection of the descriptors (DeCS) - keywords for recovering subjects from scientific literature and free terms (TL) - terms not found in MeSH and DeCS, but with relevance to the research.

In Medline, using the research engine PubMed, it was carried out a research strategy using the syntax: "smell" (DeCS) OR "olfaction disorders" (DeCS) AND "laryngectomy" (DeCS) AND "taste" (DeCS) OR "taste disorders" (DeCS); and "smell" (DeCS) OR "olfaction disorders" (DeCS) AND "laryngectomized" (TL) AND "taste" (DeCS) OR "taste disorders" (DeCS). In LILACS and SciELO it was used the keywords: "laryngectomy", "smell" and "taste."

## SELECTION CRITERIA

The inclusion criteria for found studies by researches in databases were: original articles (excluding editorials and case studies); having as among individuals who underwent

total laryngectomy; to broach changes in the smell and/or taste functions in this population with the unique proposition to assess these sensory functions with the use of specific tests; to be published in Portuguese, English, Spanish or Italian idioms. It was excluded studies that did not mention the smell and/or taste functions in laryngectomized at the title of the manuscript. We also excluded studies that brought in its title any proposed intervention to improve these functions in laryngectomized.

## DATA ANALYSIS

The selection of the articles found with the research in different databases was performed in three steps. In the first step it was carried out the reading of the articles titles. We excluded those that clearly did not fit any of the criteria for inclusion in this study. In the second step it was carried out the reading of abstracts of the selected studies in the first step and, similarly, we excluded those that clearly did not fit any of predetermined criteria of inclusion in this review. In the third step, all the studies that were not excluded in these two first steps were read in full for the selection of those who may be included in this review.

In Medline database, by PubMed, crossing the keywords and free terms, there were found 79 articles, of which 30 publications were excluded because the title, among these 09 studies that being rehabilitation proposal, 49 abstracts were read; and 23 articles were selected for full reading. It also excluded one article of the same content and authorship, with dual publication in journals and different years, being in this case considered the oldest manuscript<sup>(9)</sup>, first published. In the LILACS and SciELO databases it were found five publications, all of which were excluded for the title.

Considering the criteria for inclusion and exclusion, only 16 articles were chosen to participate in this systematic review. Three publications were excluded because they were not classified as original articles and four other articles were repeated (Figure 1).

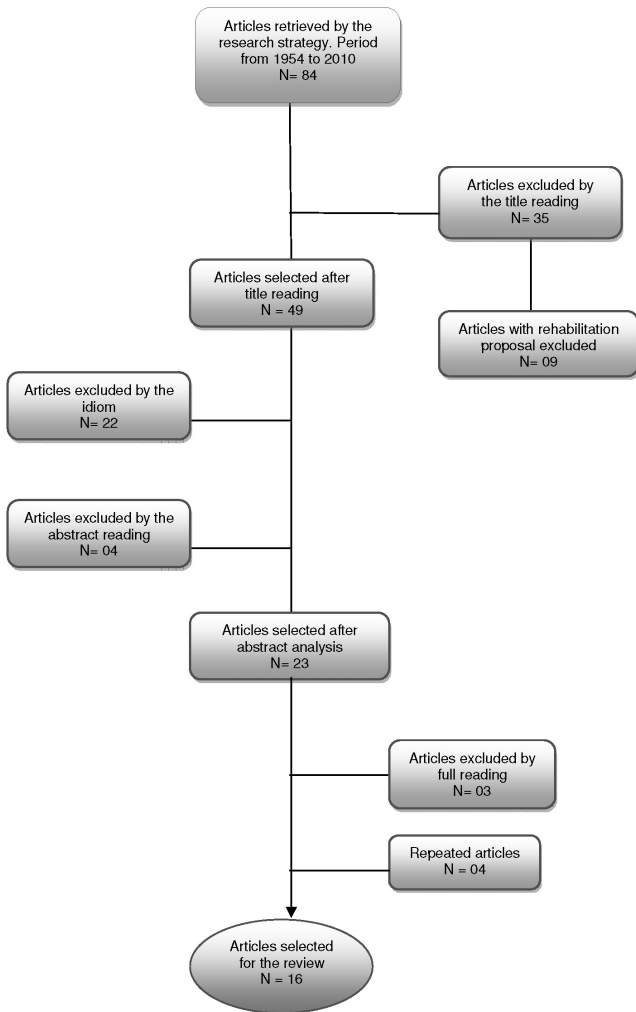
The methodological characteristics of the articles were broached according to the randomization, as well as the inclusion criteria, statistical analysis and statistical comparison between groups of selected studies (Chart 1).

In research of literature data it was found only one study that proposed that random allocation<sup>(10)</sup> in interest group and in the control group, although we not having had the intention to examine any technical intervention in this population. So, there were not found sufficient data to conduct a meta-analysis, because the heterogeneity of the articles did not allow the group through statistical analysis. Thus, the results of this study will be in the systematic review form, without meta-analysis. According to Cochrane<sup>(11)</sup>, in situations that can not make a meta-analysis the researcher should feel encouraged by the line of research in building a field randomized clinical trials.

For better presentation of results we chose to consider the following selected articles variables: author/year, country, sample, average age, time after laryngectomy, test used to evaluate the smell and/or taste functions and results (Chart 2).

**RESULTS**

The heterogeneity of the articles might be perceived in relation to periods of their publishing, emphasizing that since its



**Figure 1.** Flowchart from the number of articles found and selected after application of inclusion and exclusion criteria, according to the descriptors and databases

**Chart 1.** Methodology classification of selected articles

	Leon et al., 2007 <sup>(25)</sup>	Miani et al., 2003 <sup>(24)</sup>	Fujii et al., 2002 <sup>(23)</sup>	Welge-luessen et al., 2000 <sup>(22)</sup>	van Dam et al., 1999 <sup>(21)</sup>	Tatchell et al., 1989 <sup>(20)</sup>	Tatchell et al., 1985 <sup>(10)</sup>	Mooregillon, 1985 <sup>(19)</sup>	Kashima et al., 1979 <sup>(18)</sup>	Nieto Cortijo, 1972 <sup>(17)</sup>	Henkin et al., 1972 <sup>(16)</sup>	Hoye et al., 1970 <sup>(15)</sup>	Henkin et al., 1968 <sup>(12)</sup>	Ritter et al., 1964 <sup>(13)</sup>	Bartalena, 1958 <sup>(14)</sup>	Marco et al., 1954 <sup>(9)</sup>
1. Specified inclusion criteria	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Control group	Yes	Yes	No	No	No	No	Yes	No	No	No	No	Yes	No	Yes	No	No
3. Random allocation	No	No	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No
4. Secrecy in allocation	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
5. "Blind" subjects	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
6. "Blind" therapists	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
7. Statistical analysis	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No	No	No
8. Statistical comparison between groups	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No	No	No

first publication in 1954<sup>(9)</sup> until the end of the 60 decade there were few articles on this subject<sup>(12-14)</sup>. The increase in the production of the manuscripts could be evidenced in the 70 and 80 decade<sup>(10,15-20)</sup>, occurring thereafter a period of no publications with only retaked in 1999<sup>(21)</sup> and in 2000 years<sup>(22-25)</sup>, although with little emphasis and in discontinuous periods.

It is observed that since the beginning of the publications until the end of 80 decade was concerned to demonstrate the occurrence of reduced smell and taste acuity in laryngectomizeds, as well as the mechanisms and structures involved in these changes, using not standardized tests to investigate these sensory functions.

It is believed that in the 90 decade the decrease in studies with this proposal was due to some of these findings, since currently articles production covering this subject are directed to intervention strategies, and although these articles bring specific quantitative assessments of these functions, these analyses are only used to measure the effectiveness of rehabilitation methods<sup>(1,6,26-29)</sup>.

Another relevant point was the predominance of United State publications (50%)<sup>(10,12,13,15,16,18,20,25)</sup> and Europe (43.75%)<sup>(9,14,17,19,21,22,24)</sup>, highlighting Spain (12.5%)<sup>(9,17)</sup> and Italy (12.5%)<sup>(14,24)</sup>, without research in Latin America.

It was verified, in research about the global cancer statistic, the high risk of developing laryngeal cancer in countries located in Southern Europe, especially Italy and Spain<sup>(30)</sup>, which may explain the prevalence of studies in this continent countries.

The absence of publications in Latin America suggests, in Brazil, little approach in quantitative studies of the smell and taste functions in laryngectomized population, although it has been found an article by Brazilian researchers outside of these research strategies criteria of inclusion and exclusion adopted<sup>(31)</sup>.

In the United States realized the organization of researchers groups who follow this laryngectomized population in the resort investigation of the smell and taste functions, with publication of manuscripts in different years<sup>(10,12,15,20)</sup>. This North American concern can be related to high findings of cancer prevalence in this country<sup>(32)</sup>.

In Brazil, it is noted that researchers have given greater em-

**Chart 2.** Studies that characterize and evaluate the smell and taste functions in total laryngectomized

Author/Year	Country	Sample	Age mean, in years	Time after laryngectomy	Used test to evaluate the smell and/or taste functions	Results
Leon et al., 2007 <sup>(25)</sup>	USA	36 (04 women and 32 men) 36 control	66,8	0,5 – 25 years	Ortonasal olfact test; CCCRC; Test of retronasal olfact with diferents flavored powders based on Heilmann test	↓ olfactive function after LT; ↓ ability to smell; ↓ gustations in self-assessment
Miani et al., 2003 <sup>(24)</sup>	Italy	10 (02 women and 08 men) 10 control	45	1 – 5 years	Odor detection test with five dilutions in series based on the van Dam et al. <sup>(21)</sup> test; Olfactory epithelium biopsy	↓ olfactive perception; Occurrence of various degrees of epithelial degeneration constituting serius damage to the neuroepithelium
Fujii et al., 2002 <sup>(23)</sup>	Japan	29 (03 women and 26 men)	68,7	-	JSO; Alinamin test; Olfactory mucosous endoscopy	Threshold for detection/identification of odors tends to ↑ after 3 months and ↓ after this period; Atrophy of the nasal mucous after 12 months of LT; Apparently normal olfactory mucous
Welge-luessen et al., 2000 <sup>(22)</sup>	Germany	25 (05 women and 20 men)	63	5,75 years	SStb; CSEPs	18 with anosmia and 7 with hiposmia in psychophysical test; There was no significant correlation between the psychophysical and aelectrophysical data
van Dam FS et al., 1999 <sup>(22)</sup>	Netherlands	63 (12 women and 51 men)	66	5,1 years	Odors detection test “; Odors diferenciation test; QOTA; Semistructured interview	68% of pacients are not able to sense odors; Pacients with anosmia reported worse taste and more intense reduction of gestation and appetite
Tatchell et al., 1989 <sup>(20)</sup>	USA	25	61,9	-	Limiyary olfactive detection test (butanol) and common odors identification test and trigeminal stimulation; Mercury Nasal Resistance Meter; LB	Pacients with esophageal speech that reached a good speech remained greater olfactive sensitivity
Tatchell et al., 1985 <sup>(10)</sup>	USA	25 25 control	-	-	Limiyary olfactive detection test (butanol) and common odors identification test and trigeminal stimulation; Mercury Nasal Resistance Meter; LB	Olfactive abilities depend on nasal airflow; intact mechanism of smell function when recovered nasal airflow
Moore-Gillon, 1985 <sup>(19)</sup>	Engalnd	33 (A n=10; B n = 23)	57 A; 59 B;	Between 1 to 15 years B;	Biopsy of the superficial structure of the nasal mucous; Nasal mucociliary transport test; pyridine vapour method	Densely ciliated epithelium and mucociliary transport faster in laryngectomized compared to preoperative; Olfactive sense relatively normal in laryngectomizeds
Kashima et al., 1979 <sup>(18)</sup>	USA	123	-	Between 0 to 12 months	“Three-drop, forced-choice” technique <sup>β</sup> Test of flavor detection and identification of three diferent concentrations with sweet, salty, bitter and sour	Absence or severe change in taste after laryngectomy Gradual improvement of function in those who had not recurrent tumors
Nieto Cortijo, 1972 <sup>(17)</sup>	Spain	5 men	60,2	Between 3 months and 20 months	Histologycal study of mucous membrane of the nasal respiratory	Involuntal tendency of the nasal mucous membrane simultaneously with ↑ of the threshold olfactive and ↓ of olfactive sensitivity
Henkin et al., 1972 <sup>(16)</sup>	USA	4 (01 woman and 03 men)	41,75	0 to 8 years	“Three-drop, forced-choice” technique <sup>β</sup>	Resection of bilateral laryngeal nerves is associate to onset hiposmia;
Hoye et al., 1970 <sup>(15)</sup>	USA	52 (17 SE; 35 L) 35 control	49,1 SE; 57,8 L	01 to 8 years	Recognition and identification test; Vaporization odors in the nasal cavity	After surgery all pacients had ↓ of olfactive function; For detection of odors were used accessory olfactive areas innervated by the 5°, 9° and 10° cranial nerves
Henkin et al., 1968 <sup>(12)</sup>	USA	35 (05 women and 13 men)	58,6	0,1 a 8 years	“Three-drop, forced-choice” technique <sup>β</sup> ; Recognition and identification of flavors test	All patients reported decreased olfactive acuity; Hiposmia is present shortly after the L; None of teh patients recognized the pure taste of banana and few recognized the taste of pure orange
Ritter et al., 1964 <sup>(13)</sup>	USA	10 men 10 control		1 to 18 years	Vaporization odors in the nasal cavity	Recognize 70% of the odors presented; The olfactive ability is preserved even with desuse
Bartalena, 1958 <sup>(14)</sup>	Italy	18 a 25 b 20 c	36 a 77	7 days to 5 years	a) test with diferents purê olfactive substances; Teste olfactive-trigeminal; teste olfactive-trigeminal-gustative; b) hematogenic olfact; c) nasal cavity pH	Anosmia occurs after L and can be perceived by the decreased efficiency of nasal receptors; Anosmia is most evident through the hematogenous stimulation
Marco et al., 1954 <sup>(9)</sup>	Spain	44 (01 woman and 43 men)	57-58	Dec/1945 to Jan/1953	Elsberg technique; Subjective test of olfactive and gustative perception; Exploration of I cranial nerve through intravenous; Sensitivity gustative test	Subjective test: ↓ sensitivity of smell and taste; Olfactive test: 20 with ↓ olfactive sensitivity and 5 with anosmia; Taste test: normal in all; Intravenous: 50% positive response

**Legend:** LT = Total Laryngectomy; SE = Withdrawal paranasal sinus; L = laryngectomy; A = (A group) preoperative; B = (B group) laryngectomizeds; a = group with 18 subjects; b = group with 25 (18a + 7 subjects); c = group with 20 subjects; CCCRC = Connecticut Chemosensory Clinical Research Center; JSO = Japan Rhinology Society, 1998 – based on T&T olfactometer; SSStb = Sniffin Sticks test battery; CSEPs = Chemosensory Evoked Potentials; QOTA = Questions on Odor, Taste and Appetite; LB = Larynx bypass; “ = Derived of “Phonyl Ethyl Alcohol Single-staircase odor detection” test described by Doty e Kobal (apud van Dam et al.)<sup>(21)</sup>; <sup>β</sup> = Detection and identification of pyridina, tiopheno, nitrobenzeno, Amyl acetate e camphora vapours determined by the technique described by Henkin “the three-drop, forced-choice technique”<sup>(36)</sup>

phasis in studying issues related to quality of life and sometimes deal with a subjective way the smell and taste functions, without using specific tests for sensory investigation, understanding that these changes functions in association to another variables can cause a negative impact on quality of life of laryngectomized individuals<sup>(33,34)</sup>.

The sampling was another relevant aspect shown in manuscripts, that although there are two articles with a small number of subjects (four and five)<sup>(16,17)</sup> and another with an exacerbated number of participants (123)<sup>(18)</sup>, it was identified a prevalent variation between 25 and 35 individuals. It is assumed that this small number of individuals presented in the studies may affect the reproducibility of these findings for the general population.

In the articles selected for this review, the age of subjects analyzed was approximately 60 years, which is consistent with studies that indicate the age group 40 to 70 year as the most prevalent age for laryngeal cancer<sup>(35)</sup>.

Another point that should be taken into account in analyzing the presented results is the time of surgery, being this time varied from zero to 25 years, thus reinforcing the heterogeneity of the selected studies.

The used tests in most examined studies (62.5%) only evaluating the smell function<sup>(10,13,15-17,19,20,22-24)</sup>. It is believed that the olfactory research should be undertaken jointly with the taste function, but it is clear that there is difficulty in performing reliable and rapid tests to evaluate the taste, being mainly analyzed through tests of aqueous solutions and subjective items<sup>(9,12,14,18)</sup>.

The evaluation methods described in studies of this review used different techniques for detection and recognition of odors: pyridine, nitrobenzene, thiophene, amyl acetate and camphor vaporization<sup>(12,15,16,18)</sup>; hematogenous stimulation<sup>(9,14,23)</sup>; phenyl ethyl alcohol solution with di-propylene glycol<sup>(21,24)</sup>; butanol solutions<sup>(10,20,22,23,25)</sup>; vaporization of aromatic common substances<sup>(10,13,20,25)</sup>; pyridine vapors<sup>(19)</sup>; coffee, orange and lavender scent stimulus (Elsberg technique)<sup>(9)</sup>.

Most selected studies (75%) indicated that the evaluation of smell was mainly performed by non-standard tests for odors detection and identification. Recent studies that suggest some kind of intervention in this area has often used standardized tests, which reflected a greater concern with the precision of the instruments and therefore the results<sup>(1,6,28)</sup>.

Study conducted with 35 individuals proposed to detect and recognize odors from the pyridine, nitrobenzene, thiophene, amyl acetate and camphor vaporization through the "three stimulus" technique (forced choice-three stimulus sniff technique)<sup>(12)</sup>. This olfactory function assessment method was based in performed technique into subjects with adrenal cortical insufficiency<sup>(36)</sup>, was subsequently also referred to other works in the laryngectomized population<sup>(15,16,18)</sup>, this technique has been used in 25% of studies in this review.

The use of this method, although systematic, does not suggest reliability and neither practicality translates, differently from standardized tests, with well-defined scores and easy to apply.

In a recent study<sup>(5)</sup>, it was used the Sniffin' Sticks test, which consists on a battery of tests with odors contained in "pens",

presenting itself as a standardized test of easy reproducibility and administration, suggesting greater confidence in the results presented. But the diversity of languages and cultures has sometimes hampered the use of this test, which implies the need for translation and cultural adaptation of the instrument.

The Brief Smell Identification Test (B-SIT) is another standardized test, accepted commercially, used to evaluate olfactory function<sup>(37)</sup>. Have been recently developed a new version of this tool specifically for the Brazilian population<sup>(38)</sup>, which can be a stimulus for production of studies in laryngectomized population in Brazil.

Overall, 68.75% of the articles in this review<sup>(9,12,14-17,21-25)</sup> reported a clear decrease in olfactory acuity after submission to total laryngectomy, and all articles that proposed to study the gustatory function, attested reduction in this function after surgery<sup>(9,12,21,25,27)</sup>. But it is clear that there is no consensus among the factors that determine these sensory changes, especially in older studies. Currently it is considered that these changes may be caused by the laryngectomy due to the interruption that occurs in the respiratory tract, as well as by changes in epithelial structure of the nasal mucous.

In a study with 25 subjects it was shown in their results that the olfactory abilities depends on the nasal airflow, referring that after the restoration of this stream this function should remain intact<sup>(10)</sup>.

The histological investigation of the olfactory mucous in a research involving ten subjects, indicates that the decline of olfaction in laryngectomized seems related both to the disconnect between the upper and lower airways as well as degenerative diseases affecting the olfactory epithelium<sup>(24)</sup>.

In contrast a study by researchers at the University of Michigan shows that olfactory ability is not changed even with disuse in laryngectomized<sup>(13)</sup>. These findings corroborate with a study conducted in England<sup>(19)</sup> in which it describes the olfactory acuity within normal limits, although there are structural changes in the olfactory epithelium in laryngectomized.

The precariousness of specific tests and effective techniques may reflect those findings, as can be seen in more recent studies the presence of undeniable olfactory changes in this population<sup>(22,25)</sup>, evidenced by studies concerning rehabilitation strategies<sup>(6,26)</sup>.

Researchers in Japan<sup>(23)</sup> suggest that the olfactory acuity depend on time after laryngectomy, highlighting in study that the smell function initially worsening after the first three months of total laryngectomy submission and then tends to improve to a level almost before surgery, referring also to the olfactory mucous remains apparently normal.

In respect to the taste function there is a lack of studies in this population, having been selected for this review only one study<sup>(18)</sup>, which proposed specific analysis by the taste test with graded concentrations of aqueous solutions of salt (NaCl), sweet (sucrose), bitter (urea) and sour (HCl). Four other articles had analyzed the taste function in association to the smell function<sup>(9,12,21,25)</sup>, and in these studies they denoted a major concern to smell function.

The consequences on the smell function rather than the study of taste function in this population might instigate the

various hypotheses. The first is that as the smell is linked to breath, and breathing mode (way) is modified in these individuals, studies that shown the laceration of smell seem to merit more attention from researchers. Another possibility is that perhaps the changes of taste function in total laryngectomized may be considered as a consequence of changes in olfaction.

Thus, studies that help understand the taste function in this population should be encouraged mainly demonstrating the need for tools. In this review there is a lack of objective tests and systematic methods to evaluate this function, in order that the taste function investigation mostly be based on aqueous solutions tests, as well as questionnaires and semi-structured interviews.

Interesting instruments that evaluate the taste function can be used in research as proposed by a German researcher<sup>(39)</sup>, in which solutions with predetermined concentrations of sweet taste (sucrose), salty (sodium chloride), bitter (quinine sulfate) and sour (citric acid) are administered gradually over strips of filter paper, and this study proposed a systematic method and easy to use, so it can be reproduced.

These results underscore the need for more detailed studies in this population, considering the diversity presented, by investing in systematic methods and standardized tests.

## CONCLUSION

In this review, most studies attests to the occurrence of decreased of smell and taste sensory functions in individuals who underwent total laryngectomy. Although there is consensus regarding the damage caused by the disruption in these functions of the nasal airflow, is not yet possible to show in detail the mechanisms and structures involved, especially with regard to changes in the olfactory mucosa.

There is greater concern in the analysis of olfactory function than the taste function, considering that the changes in taste function in total laryngectomized is a consequence of changes in olfaction.

To evaluate the smell function older articles used non-standardized tests, while more recent publications were concerned to use quantitative tests protocols. While for evaluation of taste function all articles proposed non-standard assess, which may lead to less accurate in results presented.

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