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ORIGINAL ARTICLE

Long Term Serious Olfactory Loss in Colds and/or Flu☆

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KEYWORDS
Smell;
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Abstract
Introduction: In the general population, we can find 2%–3% of lifelong olfactory disorders (from hyposmia to anosmia). Two of the most frequent aetiologies are the common cold and flu. The aim of this study was to show the degree of long-term olfactory dysfunction caused by a cold or flu.
Methods: This study was based on 240 patients, with olfactory loss caused only by flu or a cold. We excluded all patients with concomitant illness (66 patients), the rest of patients (n = 174) consisted of 51 men (29.3%) and 123 women (70.7%). They all underwent olfactometry study (I and V cranial nerve) and a nasal sinus computed tomography scan, as well as magnetic resonance imaging of the brain. Results were compared with a control group (n = 120).
Results: Very significant differences in levels of olfactory impairment for the olfactory nerve ($P<.00001$) and trigeminal nerve ($P<.0001$) were confirmed.
Conclusions: People who suffer olfactory dysfunction for more than 6 months, from flu or a cold, present serious impairment of olfactory abilities.

PALABRAS CLAVE
Olfato;
Olfatometría;
Resfriado;
Gripe;
Alteraciones del olfato;
Barcelona Smell Test

Resfriado-gripe: pérdida grave del olfato a largo plazo

Resumen
Introducción: Las personas afectadas por pérdida olfativa total y de por vida se sitúan entre el 2 y el 3% de la población. Dos de las causas más frecuentes son los resfriados comunes y las gripes. El objetivo de este trabajo es mostrar el grado de afectación de las alteraciones olfativas sufridas, a largo plazo, a causa de un resfriado o una gripe.
Métodos: Este estudio se ha basado en la asistencia a 240 pacientes, aquejados de pérdida olfativa por resfriado o gripe. Fueron excluidos todos aquellos que padecían otras enfermedades

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intercurrentes (66 pacientes), el resto (n = 174) estaba formado por 51 hombres (29,3%) y 123 mujeres (70,7%). Fueron sometidos a estudio olfatométrico (I y V par craneal) y tomografía axial computarizada nasosinusal, y resonancia magnètica del sistema nervioso central (RM-SNC) comparándose el resultado con un grupo control (n = 120).
Resultados: Se confirmó que la pérdida olfativa tanto para el nervio olfativo (p < 0,00001) como la alteración del nervio trigémino (p < 0,0001) eran muy significativas.
Conclusiones: La pérdida del olfato, pasados más de 6 meses desde su inicio supone una reducción grave de las capacidades olfativas de las personas afectadas.

Introduction

Survey studies on the general population affected by olfactory pathology show that disorders in the sense of smell reach 19% of the population, ranging from 0.5% for anosmic individuals and 17% for hyposmic individuals, depending on whether you take international or local studies[1,2]; for absolute loss of the sense of smell alone, the variation ranges from 2% to 3%. Among the most frequent causes are the common cold and flu.

The world-wide annual number of viral rhinitis causing cold and flu could be approximately 20 billion cases, all caused by both the cold virus (rhinovirus) and the flu virus (influenza).[3] Not all of them have been diagnosed from the viral point of view. In Spain an incidence index is currently foreseen of 66.88 cases/100,000 inhabitants.[4]

The high levels of particles of human parainfluenza type 3 virus (HPIV3) found in the epithelial cells of the nasal turbinates of patients with postviral hyposmia suggest that HPIV3 is the cause of the postviral olfactory disorders.[5] The true affectation of the population is much greater than the analytical verifications performed.

Patients whose olfactory problems are triggered after an infectious condition of the upper airway report distortion of smells.[6] They generally refer to, due to cultural semantic reasons, as a loss of ''taste'' when what happens, in over 80% of these individuals, is that they present only the loss of the sense of smell and conserved that of taste (sweet, salty, acid, bitter, and umami). In all these patients, the majority recover their normal olfactory state, more or less quickly, but in a small segment (not negligible in absolute numbers) the partial or total loss of their sense of smell persists.

Studies indicate that viral infections of the upper airway are one of the main causes of hyposmia and that it improves in most patients when the viral symptoms resolve, but some patients present hyposmia as a sequela for months or permanently.[7,8]

It has been reported that the loss of the sense of smell from cold/flu forms part of the 39% of olfactory disorders caused by upper airway involvement.[4] It has also been indicated that, given how suddenly it is established, this loss of smell is accompanied by significant affective discomfort and loss of quality of life.[9,10]

Among the 1166 cases of olfactory disorders attended in our otorhinolaryngology (ORL) service, dysosmias due to aetiologies of colds/flu correspond to 23.6% of all the cases (Fig. 1). It is worthwhile mentioning that, in our centre, colds, and flu are the second cause of loss of sense of smell (the first is sinonasal polyposis), which is not the case in other centres.[11,12]

The dysosmia produced by colds/flu is generally differentiated by the self-report given by patients of an episode of having had a cold or flu. In some cases, this reference is not so explicit, so it has to be elicited while taking the clinical history. From the point of view of a classic ORL examination, no lesions are evident at nasal level, not even using a fibre-optic endoscope. This fact, along with the lack of specific drug therapy for such disorders, leads to this type of pathology currently being classified as untreatable, as irreversible, which is a motive for terminating attention to the patients that suffer from it, telling them ''not to waste their time because nothing can be done''.

Our study is different from the normal studies on dysosmia after a cold in that most of such studies are carried out during acute phases or in very recent flu states, while ours is carried out on the long-term olfactory state.

The objectives of this study were as follows: firstly, show that this type of affectation can produce long-term olfactory loss, even lasting for life; secondly, demonstrate that the level of affectation of the olfactory disorders suffered is important; third, show that these disorders can be demonstrated (parameterised); fourth, show that these alterations can be diagnosed; and fifth, indicate the repercussions that lack of attention brings.

Methods

To carry out this study, we started on the basis of a group of 240 patients who attended our consultation for prolonged loss of the sense of smell (15 months on average), either at their own request or recommended by their family doctors, once they had been diagnosed with flu or a cold (according to World Health Organisation guideline, in each seasonal period in the health areas in our territory, for both flu and colds). We excluded from this group the patients who suffered from other intercurrent diseases, suspected of influencing the smell disorder (66 patients), such as sinonasal polyposis, allergies, neurological disorders, head injuries, etc. The rest of the patients (n=174) consisted of 123 women (70.7%) and 51 men (29.3%). (Fig. 2a). The distribution by age corresponded to 72% of patients between 40 and 60 years, of which approximately 30% (30.5%) were 50–59 years old (Fig. 2b).

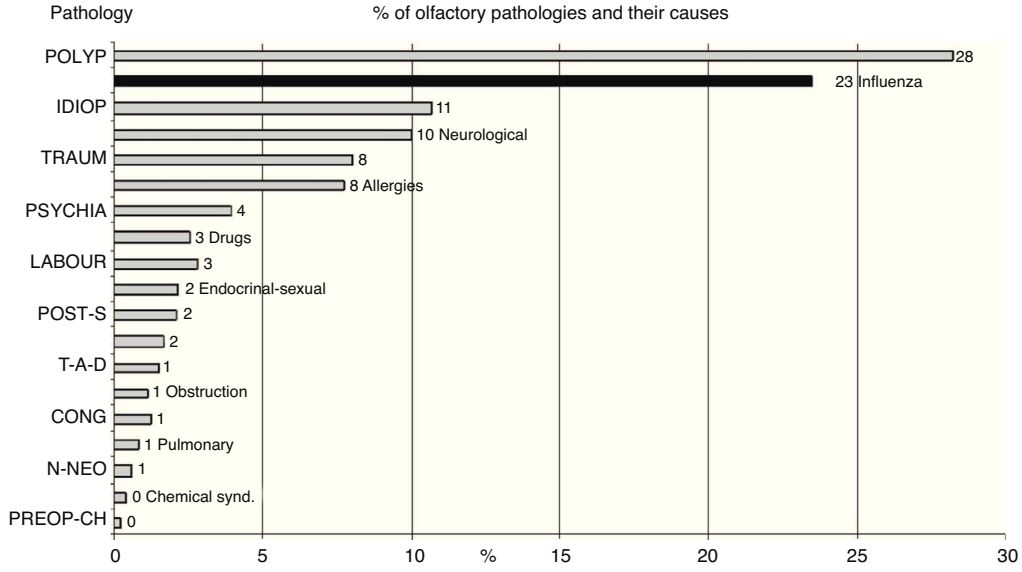

Figure 1 Olfactory pathologies handled (1166 patients), ordered from more to less frequency. These pathology consultations arose from the derivation from our primary health care centres and/or referred to our service from other hospital centres. The disorders were codified as follows: CONG (congenital), PREOP-CH (preoperative evaluation, chemical), IDIOP (idiopathic), LABOUR (labour), N-NEO (nasal neoformation), POLYP (polyposis), POST-S (post-surgical), PSYCHIA (psychiatric), T-A-D (tobacco-alcohol-drugs), and TRAUM (traumatic). It can be seen that the cause of colds/flu (black bar) is the 2nd most important, behind sinonasal polyposis and followed by idiopathic, neurological, traumatic, and allergic. It should be noted that the total percentage exceeds 100%, due to the existence of cases that involved several simultaneous aetiologies.

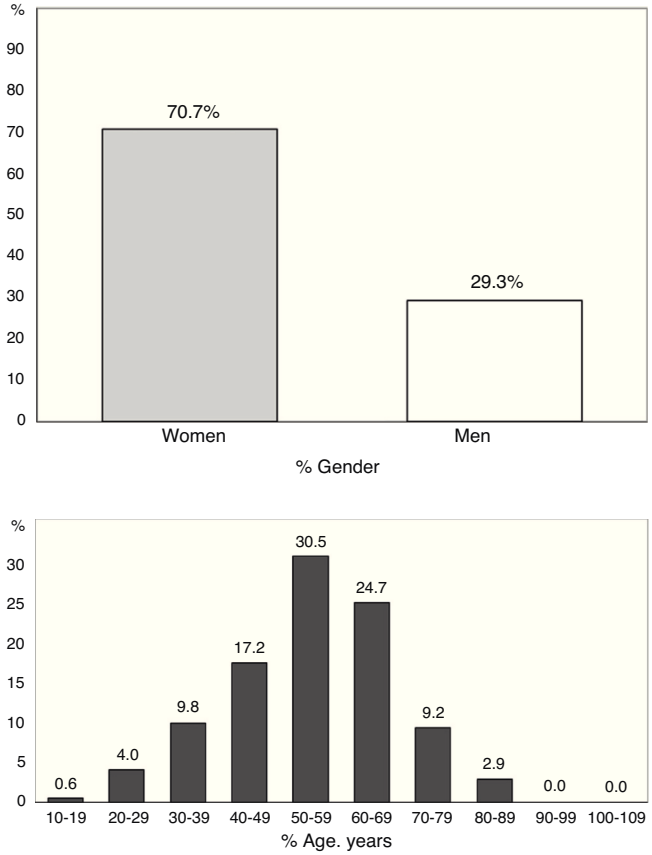

Figure 2 (a) Significant predominance of involvement of females over males in the study group patients (postviral anosmia). (b) More than 70% of the cases are found in individuals aged between 40 and 69 years.

We carried out a general anamnesis general, as well as taking a specific case history for this pathology and one for smell disorders. The condition of the sinonasal cavities was assessed by fibroscopic rhinoscopy (rigid Hopkins II 0°).

Given that there is statistical correlation between the perception of olfactory improvement and smell tests in patients with anosmia/hyposmia,[13] all of our patients were given the Barcelona smell test BAST-24,[14,15] composed of the following: 20 odours for the first cranial nerve (olfactory nerve) and 4 odours for the 5th cranial nerve (trigeminal). This type of examination is based on the forced response method,[16,17] quantitative–qualitative, based on 20 substances for the 1st cranial nerve and 4 for the 5th nerve; this makes it possible to parameterise both the capacity to perceive a smell or ''detection'' (DT) and the capacity to recognise correctly the smell presented or ''correct identification'' (CI), including the analysis of the smell characteristics and of the olfactory pathways.[18]

For the criteria of assessment of postviral loss of the sense of smell, we followed 2 analysis parameters: the olfactory parameter that qualified the degree of anosmia (quantitative, qualitative, mixed, objective, subjective, etc.) and the viral disease parameter. With the first parameter, the Seiden and Duncan[7] criteria given in 2004 were taken into consideration.

This analysis was applied to the study of the 1st and 5th cranial nerves, to verify the involvement of the sense of smell (olfactory), through the olfactory nerved, and the affectation of the rest of the sinonasal mucosa (touch), through the trigeminal nerve. The olfactory manoeuvre was performed either in both nostrils at once (simultaneously) or first in one side and then in the other (bilateral). The decision was based on the subjective patient perception of

breathing better through one nostril or the other. In the cases of bilateral study, the nostril with better olfaction was chosen, following the principle of better sensory laterality.[19]

All of the patients in the study group received a sinonasal computed axial tomography and CNS-RM assessment to rule out hidden concomitant pathologies. The study group was compared with a control group selected from the population in our environment (n=120), consisting of 60 men and 60 women, with an age range of 15–85 years and a mean age of 42 (±1.7) years. This control group was part of our database for the olfactory study, consisting of 270 people with ages from 10 years to those older than 100. The Department of Statistics and Social and Preventive Medicine performed the data analysis by a data clean-up starting from searching for non-standard or values or illogical information in the registry of incongruent answers, to ensure the quality of the database. First, they performed a univariate descriptive analysis, with the specifications of every one of the variables studied, by describing their distribution according to categories (qualitative variables) that included frequency and percentage of each category. Second, they performed a bivariate descriptive analysis between the variables that had previously been chosen because there was a reasoned justification for their possible relationship. The usual statistical techniques for comparing 2 qualitative variables were used: the Chi squared test or Fisher's exact test; The latter was used when the frequency was less than 5 in some cells. All of the statistical tests were performed with a confidence level of 95% and by bilateral contrast, using the statistical programme SPSSWIN version 9.0.

Results

The first fact to notice is the concentration of cases around the age of 50 years (critical point of maximum olfactory capacity of our olfactory physiology), with the females presenting the most involvement.

With respect to the 1st cranial nerved, it was shown that the DT capacity for the pathological group was 3 odours out of 20, detected some 70%–80% of the times; 11 odours out of 20, which were detected 60%–70% of the times; and 6 odours, detected 50%–60% of the times (Fig. 3a). However, in the control group, the majority found the DT between 95% and 100% of the times (Fig. 3b). To evaluate CI capacity, we found that none of the odours tested exceeded 30% of the times of CI in the study group (Fig. 3c), while for the control group it ranged between 50% and 100% of the CI (Fig. 3c).

Comparing the results from the group affected by colds/flu with the control group for the analysis of DT capacity, we found that the control group presented a fluctuation ranging from 99% to 100% of the times that the odours presented were detected. In contrast, the group with smell disorders produced by colds/flu scored a maximum of 70% of the times (Fig. 3b). If we apply the same comparison for CI capacity, we can see that the control group had a variation of correct identification of these same odours that ranged from 51% to 99% of the times of odours corrected recognised, while in the group with smell disorders produced by colds/flue, the maximum was only 28% of the times (Fig. 3c). Applying the statistical analysis showed highly significant figures (P<.00001).

With respect to the 5th cranial nerve (in charge of nasal touch detection), the colds/flue group continued with the same pattern that appeared for the 1st cranial nerve. Detection capacity that ranged between 40% and 75% of the times (Fig. 4a) was thus verified for the study group, while CI capacity was a maximum of 29% of the times (Fig. 4b). Comparing with the control group again yields significant results (P<.0001).

Discussion

Accepting colds and flu as normal diseases that are normally trivial influences the absence of research into their sequelae at the level of the sense of smell. In the majority of the cases, recovery from this olfactory disorder is immediate and complete, with the resolution of the viral process. However, some individuals do not reach this degree of recovery so immediately and completely. Postviral olfactory dysfunction is believed to be provoked by lesions in the olfactory receptor cells.[20,21] Consequently, it is a syndrome characterised by sudden loss of the sense of smell, after an upper airway infection. When the infection is cured, the olfactory alteration generally persists as the only nasal symptom,[22] which can present different degrees of olfactory disorder (hyposmia, anosmia, etc.). Because of this, the case history becomes crucial for its detection.

At present there are more than 200 types of virus that can cause the common cold. Most of them are difficult to identify at the moment of the ORL consultation because normally the patients involved come for consultation some time after the infection.

Rhinoviruses are the chief cause. They represent 30%-35% of the cases of cold, followed by the adenovirus, coxsackievirus, echovirus, paramyxovirus, syncytial respiratory virus, and enterovirus, with a rate of 10%–15%.[23]

With respect to the flu, it is suspected that HPIV3, which is the trigger for only 3% of viral upper respiratory infections in adults,[24] is the most aggressive of all of them insofar as smell disorders. This is because, first of all, epidemiologically HPIV3 and postviral olfactory dysfunction present similar seasonal prevalence patterns[25] and, secondly, HPIV3 was isolated in cerebrospinal fluid in aseptic meningitis, suggesting neurotropism. This reinforced the idea that HPIV3 could infect olfactory epithelium.[26] After that, it was shown that rhinoviruses provoke postviral olfactory dysfunction using mechanisms different from those of nasal obstruction and they can provoke olfactory dysfunction of different seriousness and time lapse.[27]

Whether it is through direct involvement of the upper airways or through an indirect pathway in the lower airways, from the aetiopathogenic point of view we should indicate that olfactory perception is the result of the joint activity of the 1st and 5th cranial nerves. Consequently,[28] the olfactory disorder is due as much to the lesions on the former (the most important) as to the second.[29] The reason is that the territory of nasal mucosa, whether olfactory or not, constitutes fertile ground for the evolution of the viral infections of colds and flu. The damaging mechanism of the olfactory mucosa consists of the invasion of the epithelial cells of the nasal mucosa (both olfactory and non-olfactory) by the different viruses and the posterior destruction of these cells.

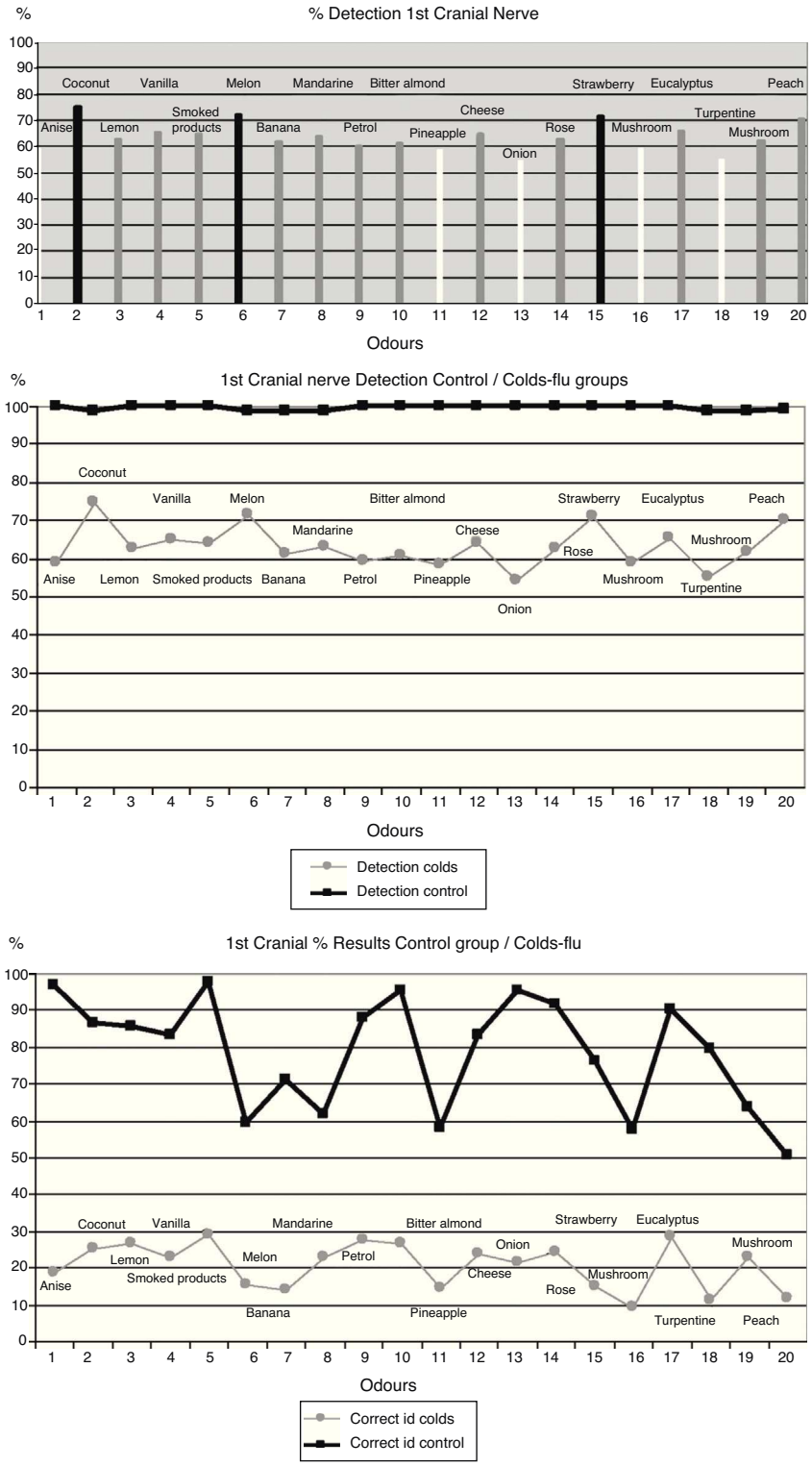

Figure 3 (a) Pathological group. In black, the odours that are seen in the surroundings (DT) above 70% of the times (coconut=2, melon=6, and strawberry=15). In grey, the odours that are perceived from 60% to 70% of the times (lemon=3, vanilla=4, smoked product=5, banana=7, mandarine=8, bitter almond=9, petrol=10, cheese=12, rose=14, eucalyptus=17, turpentine=18, and peach=20). In white, the odours perceived below 60% (anis, pineapple, onion, mushroom, and clove). These results indicate a significant reduction in the olfactory capacity with respect to the non-affected population. (b) Comparing the capability of discovering whether there is a smell in the surroundings (DT) between the control group (black line) and the colds/flu group (grey line), we observe that the control group is placed at 99%-100% of the times that they are capable of perceiving (DT). However, the pathological group is placed at 60%–70%. (c) The capability of correctly recognising the odours (CI) ranges between 50% and 98% of the times for the control group (black line), while it ranges from 10% to 29% for the pathological group (grey line).

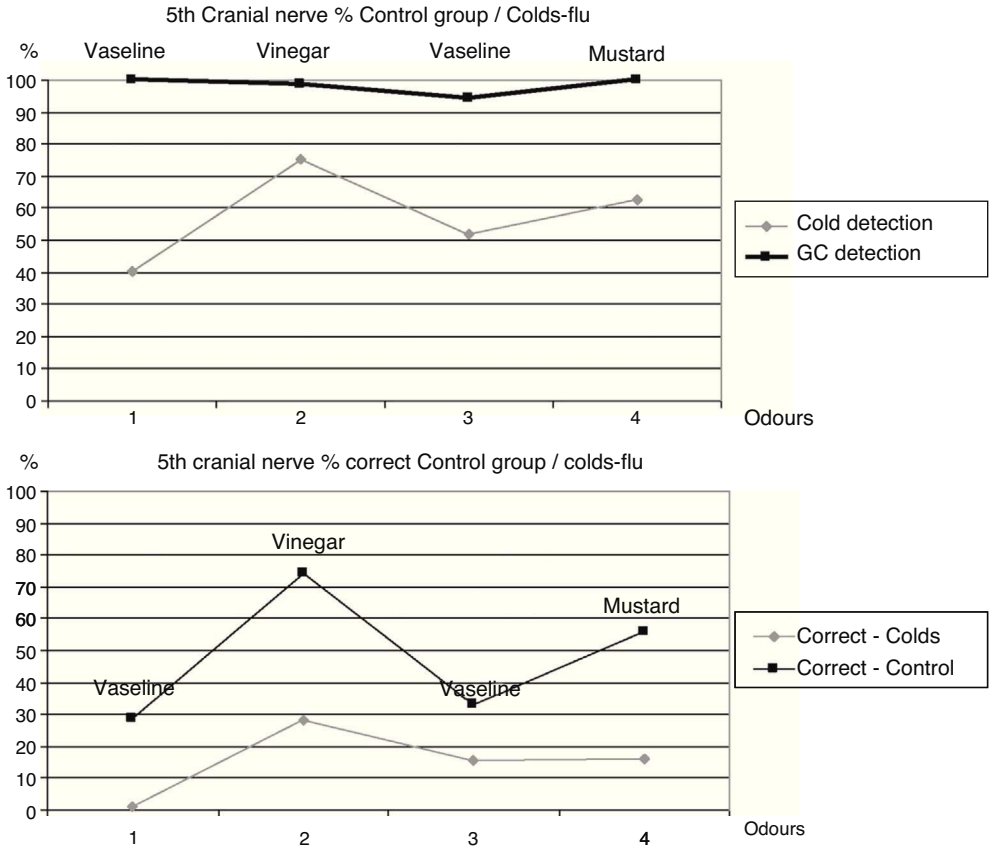

Figure 4 (a) At the level of the trigeminal nerve, for the control group (black line), the perception (DT) of odours of great trigeminal incidence ranged from 95% to 100%; in contrast, in the group with colds-flu pathology (grey line), it ranged from 40% to 75% of the times that odours were detected. (b) In the study on the capability to correctly identify (CI) odours of high trigeminal load, in the control group (black line) there was a range from 40% to 75%, of the times that they are identified correctly, while for the colds-flu group (grey line), this did not exceed 29% of correct answers.

This mechanism is the cause that leads to the loss of both olfactory epithelial cells (Schultze's cells) and non-olfactory mucosa cells (stratified epithelium), with the peculiarity that sensory terminals of the trigeminal nerve are found in both types of mucosa.

The epidemiological fact that there is a clear predominance of females in this study could be due to, on the one hand, that middle-aged women have a greater tendency to suffer smell disorders than men (with spring-summer prevalence)[25,30] and to, on the other hand, a greater tendency that women would have to take care of themselves, a motive by which there would be greater presence of females in ORL consultations.

This type of olfactory pathologies lies outside of the diagnostic reach of fibroscopy and radiology. The only way to detect them is through taking a case history and through smell examination.

As we have already indicated, smell disorders caused by colds and flu are, in our service, in the order of 24%. It is a type of loss of the sense of smell that presents greater loss of DT capability of substances in the air than, for example, inflammatory processes of sinonasal polyposis, allergy, and chronic rhinitis. The same is true in the analysis of CI capability[31,32]; the loss of the sense of smell is more serious in the colds/flu processes than in inflammations and allergies, for both the 1st cranial nerve and for the 5th.

In the normal population, the olfactory capability of individuals that have suffered a cold or flu of this type drops from 40% to 80%, more than the rest of the non-affected population.

It is easy to understand that in some people the appearance of this pathology involves a certain condition of anxiety from the suddenness and depth of its establishment, which is directly proportional to the normal use of their olfactory faculties and to their usefulness in their work and free time.

Conclusions

We can confirm that the conclusions fit the hypothesis of this study:

- It is confirmed and shown that the patient insistence on the persistence of a reduced sense of smell for a long time, much after having had a cold or flu, is true and significant.
- The involvement of both the olfactory nerve as the trigeminal nerve is demonstrated.
- The degree of affectation of the smell disorders is important and equivalent to a loss of more than 70%, so it is

necessary to speak of severe hyposmia or anosmia. Furthermore, we suspect that this loss is more than this figure, given that the assessment was performed based on the nostril that presented better sense of smell.
- We can parameterise such disorders, which can be demonstrated by quantitative, qualitative, mixed, objective and subjective systems, among others. This fact is important, given that it makes it possible to record, visualise, and follow-up on the development of these disorders. The method described here is one of these systems.
- Classic diagnosis of this type of pathologies can be expanded, to the extent that the normal model is based on only the study of olfactory variations, circumscribed to the length of time the viral process lasts and not on the long-term sequelae.
- The need for a correct, complete diagnosis that makes it possible to evaluate both the condition of the sense of smell (olfactory nerve) and its tactile function (trigeminal nerve) is posed. The importance of the diagnosis lies as much in the study of the lesions produced by the colds as in the differential diagnosis that should be performed with respect to other hidden, intercurrent pathologies such as sinonasal polyposis and allergies, or that present a much lower disorder with respect to that of viral processes, or with diseases whose first signs and symptoms are olfactory disorders, such as Parkinson's, Alzheimer's and senile degenerations (vascular, neurological).
- It should be remembered that this problem more often affects individuals aged from 40 to 69 years and, of these, those aged from 50 to 59 years, there is also the aggravating factor that females predominate with values nearly 4 times higher than those of males.
- Lastly, the repercussions of this pathology should be mentioned; they involve very important negative effects on quality of life, both in private life and work, due to the risk of accidents, disarray in hygiene, reduction of access to work, and so on.

In short, although the use of magnetic resonance scans has been encouraged as an indicator of the olfactory function,[33] to verify the modifications that have been detected in the volume of the olfactory bulb and which might be linked to the viral process, we propose that there is a need to incorporate olfactometry examination, given that the olfactory pathology is an alteration that is persistent (years) and important in the long run accompanying the post-colds/flu sequelae.

Conflict of Interest

The authors have no conflict of interest to declare.

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