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RHINOLOGY

Multiple chemical sensitivity worsens quality of life and cognitive and sensorial features of sense of smell

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Abstract Multiple chemical sensitivity (MCS) is characterized by a loss of tolerance to a variety of environmental chemicals. Multiple chemical sensitivity is frequently triggered by exposure to chemical agents, especially insecticides. The aim of the study was to measure the sense of smell and quality of life in patients with MCS compared to the control group. We studied the sense of smell, both sensitive and sensorial characteristics, in female patients with MCS ($n = 58$, mean 50.5 ± 8.5 years) and healthy female volunteers without rhinosinusal pathologies ($n = 60$, mean age 46 ± 10.2 years). Olfactometry (Barcelona Smell Test 24/BAST-24), sinonasal symptoms (visual analogue scale/VAS 0–100 mm), and quality of life (Quick Environmental Exposure and Sensitivity Inventory/QEESI) were assessed. Multiple chemical sensitivity patients showed a significant impairment in smell identification (19 ± 12 %; $p > 0.05$) and forced choice (62 ± 18 %; $p > 0.05$), but not in smell detection (96 ± 4 %) compared to the control group. Multiple chemical sensitivity patients reported more odours as being intense and irritating and less fresh and pleasant when compared with the control group. Patients scored a high level (40–100) on QEESI questionnaire (symptom severity, chemical intolerances, other intolerances, life impact). In MCS patients, total symptom intensity (VAS/0–700 mm) score was 202 ± 135, while disease severity score was 80 ± 23. The most frequent symptoms were itching and posterior rhinorrhea. Multiple chemical sensitivity patients have an impairment in smell cognitive abilities (odour identification and forced choice, but not for detection) with increased smell hypersensitivity and poor quality of life.

Keywords Multiple chemical sensitivity · Quality of life · Quick Environmental Exposure and Sensitivity Inventory · Sinonasal symptoms · Smell

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Introduction

Multiple chemical sensitivity (MCS) is defined as a subjective odour-mediated hypersensitivity towards common chemical agents in the personal environment. Multiple chemical sensitivity has a prevalence of 2–13 % in population-based surveys [1, 2]. It is a poorly understood condition characterized by multiple "medical unexplained" or "functional" symptoms that are attributed to chemically

unrelated substances in the environment at concentrations far below those toxicologically established to cause harmful effects [1, 3]. The complaints typically focus on odourant chemical agents such as car exhaust, perfumes, pesticides, paint, new carpeting, air pollution, cigarette smoke, or hair spray [4]. However, many patients also report intolerance tonon-odourant agents such as amalgam from tooth fillings and food additives, medical drugs, or alcohol [5, 6]. To date there are a number of hypotheses regarding MCS etiology including changes of the immune system, neurotoxicity, and psychological and behavior conditioning involving psycho-physiological mechanisms [7, 8].

In addition, many MCS individuals also meet criteria for other functional syndromes such as chronic fatigue syndrome, irritable bowel syndrome, and fibromyalgia [9]. Patients with MCS report symptoms related to multiple systems: nervous, cardiovascular, gastrointestinal, respiratory, genitourinary, skeletal–muscular, skin, and ocular [6].

Only few studies have analysed the impact of MCS on the sense of smell [10, 11]. To our knowledge there are no further studies about the effect of odours on smell perception and recognition. The main aim of this study was to investigate smell features (cognitive and sensorial), nasal reactivity, and quality of life in female patients with MCS compared to the general population.

Materials and methods

Study population

All patients were recruited from the Toxicology Unit and met the 1999 Consensus Criteria defining MCS as a chronic condition, with symptoms that recur reproducibly in response to low levels of exposure to multiple unrelated chemicals, improve or resolve when incitants are removed, and occur in multiple organ systems [12]. The same otorhinolaryngologist of the Rhinology Unit and Smell Clinic (ENT Department, Hospital Clínic de Barcelona) evaluated all patients. The ethics committee of our institution approved the study and signed informed consent was obtained from all patients. Sixty-two diagnosed MCS patients were enrolled in this prospective study. Four patients were excluded for different causes: mild nasal polyposis ($n = 1$), chronic rhinosinusitis ($n = 1$), and smell test intolerance ($n = 2$). Finally, 58 female patients met the study inclusion criteria.

Healthy volunteer females ($n = 60$) matched by age without MCS or rhinosinusal pathologies were enrolled as the control group. Nasal endoscopy showed no significant differences between MCS and volunteers regarding mucosa colour, turbinal hypertrophy, or septum deviation.

Inclusion and exclusion criteria

Females older than 18 years with MCS were included in this study. Patients with chronic rhinosinusitis and/or nasal polyposis, allergic rhinitis, intranasal drug abuse, nasal surgery, or past history of pre-existing subjective smell disturbance were excluded. To exclude nasal pathologies, nasal endoscopy using a rigid endoscope was performed in all patients.

Study outcomes

Smell test

Subjective olfactometries for clinical use have been developed in different countries, but no single test has gained general acceptance. The authors have developed the Barcelona Smell Test 24 (BAST-24) as a validated and reliable method to assess olfactory function in clinical practice for the Spanish population [13–16]. BAST-24 consists of 24 odours and, after being exposed for 5 s to an odour, patients were asked to answer a number of questions: (1) smell detection: "did you smell anything?"; (2) smell identification: "did you recognize this odour?"; (3) smell intensity: "was this odour intense?"; (4) smell irritability: "was this odour irritating?"; (5) smell freshness: "was this odour fresh?"; (6) smell pleasure: "was odour pleasant?"; (7) smell forced choice (to choose one from four possible): "which of these four odours did you smell?". The test was repeated for each of the 24 odours. For all smell characteristics, the total score ranged from 0 to100 % to compare it with the Spanish population.

Quick Environmental Exposure and Sensitivity Inventory (QEESI)

Quick Environmental Exposure and Sensitivity Inventory is a reliable, 50-item, valid self-administered questionnaire that was developed to gauge the multisystem symptoms and multiple intolerants often reported in MCS [5]. The Spanish version has also been evaluated in terms of validity and reliability [17, 18]. The instrument has five scales: symptom severity, chemical intolerances, other intolerances, life impact, and masking index (ongoing exposures from routinely used products). Four of the QEESI scales consist of ten items where responses range from "not at all a problem" (0) to "disabling symptoms" (10), resulting in a score range from 0 to 100. The fifth scale, the masking index, also consists of ten items, but the response format is (0 or 1), resulting in a score range from 0 to 10. Miller and Prihoda (1999) defined the criteria for three levels of symptom score as low (0–19), medium (20–39), and high (40–100).

Sinonasal symptoms

Patients were asked to score their sinonasal symptoms (nasal obstruction, facial pain or pressure, anterior and posterior discharge, sneezing, itching, and loss of smell) and MCS severity using a visual analogue scale (VAS, 0–100 mm). A total of seven sinonasal symptoms (T7SS, 0–700 mm) were also scored.

Statistical analyses

The data are presented as mean ± SD (standard deviation). All data were assessed for normal distribution and the Bonferroni correction for multiple comparisons was used. Student's *t* test was used to compare outcomes with those of the healthy population. $p < 0.05$ was considered to be statistically significant.

Results

Fifty-eight female patients with MCS (mean age 50.5 ± 8.5 years) and 60 healthy female matched by age (mean age 46 ± 10.2 years) were included in the present study. In the MCS group, the following conditions were identified: chronic fatigue syndrome (CFS) (79.3 %), fibromyalgia (62.1 %), depression (60.3 %), hypothyroidism (10.3 %), and hyperthyroidism (8.6 %). The origin of the syndrome was related to occupational exposure to a variety of chemical agents (fumigation of the workplace with insecticides, occupational exposure to household cleaning products, etc.) in 34 cases (58.6 %). In 24 patients (41.4 %) the MCS was not associated with any toxic exposure and was considered a manifestation of their comorbidities.

Smell test (BAST-24)

Multiple chemical sensitivity patients showed a significant impairment on smell identification (19 ± 12 %; $p > 0.05$) and forced choice (62 ± 18 %; $p > 0.05$), but not for detection (96 ± 4 %) compared to the control group (55 ± 23, 76 ± 17, 99 ± 2 %, respectively) (Fig. 1). Multiple chemical sensitivity patients reported more odours as intense (62 ± 16 %; $p < 0.05$) and irritating (54 ± 28 %; $p < 0.05$), but less fresh (26 ± 18 %; $p < 0.05$) and pleasant (30 ± 20 %; $p < 0.05$) when compared with volunteers (53 ± 15, 35 ± 17, 41 ± 17, 56 ± 12 %, respectively) (Fig. 2). Separate statistical analysis of patients with CFS, fibromyalgia, or other comorbidities demonstrated no further accumulative negative impact on the sense of smell of patients with MCS.

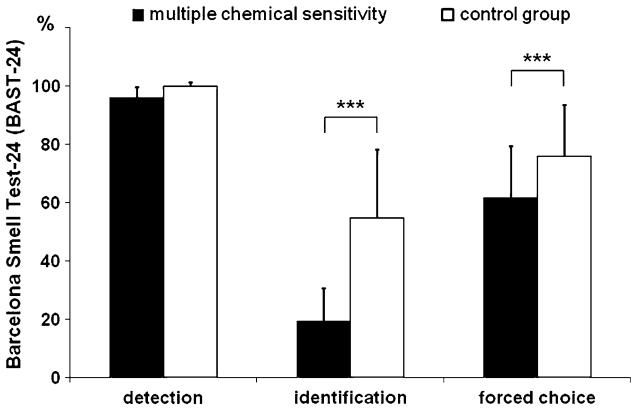

Fig. 1 Cognitive characteristics of smell test in patients with multiple chemical sensitivity; ***$p < 0.0001$ compared to the healthy control group

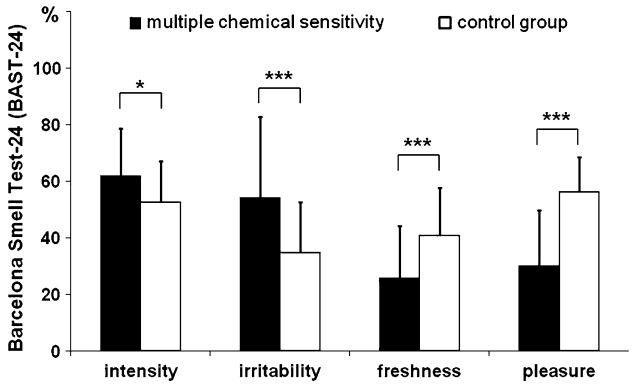

Fig. 2 Sensorial characteristics of smell test in patients with multiple chemical sensitivity; *$p < 0.05$ and ***$p < 0.0001$ compared to the healthy control group

QEESI questionnaire

All MCS patients scored at high level (40–100) in QEESI questionnaire (symptom severity, chemical intolerances, other intolerances, life impact) except for masking index that showed a higher positive response among the control group compared to MCS (Fig. 3). The masking index scale measures avoidance behaviors that the patient displays as his MCS progresses, since adding negative responses relate to the presence of the disease. No correlations were found between impairment of smell (BAST-24) and quality of life (QEESI scales).

Sinonasal symptoms

The VAS T7SS was 202 ± 135, while MCS was 80 ± 23. The most frequent symptoms were nasal itching and

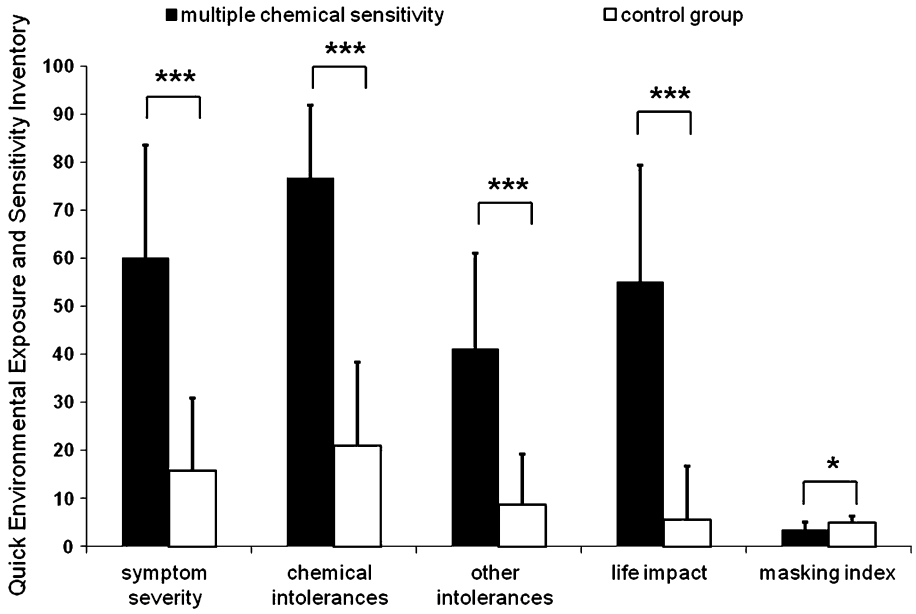

Fig. 3 Quick Environmental Exposure and Sensitivity Inventory in patients with multiple chemical sensitivity; *$p < 0.05$ and ***$p < 0.0001$ compared to the healthy control group

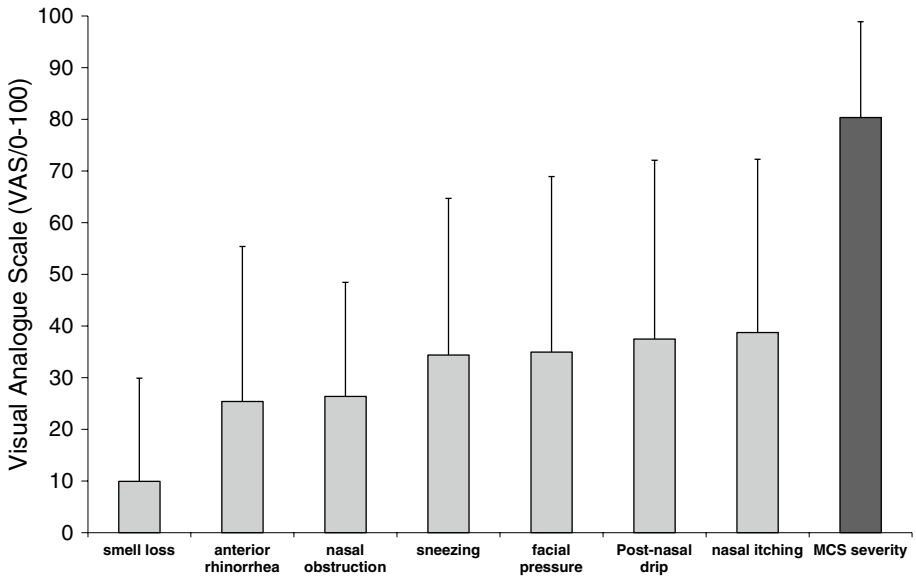

Fig. 4 Sinonasal symptoms and disease severity scored by visual analogue scale in patients with multiple chemical sensitivity; *$p < 0.05$ and ***$p < 0.0001$ compared to the healthy control group

post-nasal drip followed by facial pressure, sneezing, nasal obstruction, anterior rhinorrhea, and smell loss (Fig. 4). There was a positive correlation between T7SS and QEESI score (symptom severity) ($r = 0.45$, $p < 001$).

Study limitations

The main limitations of the study were: (1) BAST-24 does not incorporate the odour detection threshold test, which could also be useful to measure olfactory acuity; and (2) most smell tests are dependent on patient compliance ("subjective" methods).

Discussion

The main findings of our study were: (1) MCS patients have impairment of smell cognitive abilities (identification and forced choice), but not detection; (2) nasal hypersensitivity to perceive odours as more intense and irritating, but less fresh and pleasant; and (3) impairment of quality of life.

Our results are in agreement with Caccappolo et al. who reported MCS patients demonstrated no greater ability to identify odours using the University of Pennsylvania Smell Identification Test (UPSIT) or to detect odours at lower concentrations (phenylethyl alcohol and pyridine) than did

age- and gender-matched healthy controls or other patient groups with asthma or chronic fatigue syndrome [10]. In addition, Ojima et al. demonstrated, using UPSIT, that MCS subjects were able to identify odours equally as well as the controls, but found a larger number of odours to be unpleasant than controls [11]. However, using odour detection thresholds for 2-phenylethyl alcohol (a major component of rose oil) and methyl ethyl ketone (a common solvent), Doty concluded that patients complaining of MCS do not evidence higher olfactory threshold sensitivity than matched healthy controls [19].

Regarding chemosensory perception and odours' pleasantness, our results were similar to Nordin et al. [20]. Our patients perceived odours as being more intense and irritating, but less fresh and pleasant. However, Nordin's patients perceived pyridine as more intense, less pleasant, and more irritating than controls. Moreover, a recent study has indicated that high environmental chemosensory responsiveness may predict higher odour intensity ratings, while low olfactory thresholds (high sensitivity) may predict lower pleasantness ratings. Overall, unpleasant odours were perceived as more intense [21].

Concerning quality of life, MCS patients reported significantly higher scores on the QEESI subscales for chemical intolerances, other intolerances, symptom severity, and quality of life impact. However, they showed lower score for masking factors that might otherwise obscure awareness of an association between chemical exposures and symptoms. Only few studies have used QEESI instrument while confirming the same results [23, 24]. The severity of olfactory dysfunction measured by VAS or smell test did not correlate with QEESI.

Future studies examining the impact of MCS upon olfaction using objective measures (olfactory evoked potentials, functional magnetic resonance imaging, functional positron emission tomography) would be of interest.

Conclusion

Our study demonstrates that MCS patients show an impairment of smell cognitive abilities (identification and forced choice) but not detection, a nasal hypersensitivity to perceive odours as more intense and irritating but less fresh and pleasant, and impairment of quality of life.

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