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MINI-REVIEW

Anesthesia in patients with multiple chemical sensitivity: current understanding

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Abstract

Multiple Chemical Sensitivity (MCS) is a pathological condition that we do not yet have a clear understanding of from an etiological and clinical point of view. The underlying mechanisms of the disorder are still being investigated and the most frequently reported symptoms by patients are malaise, fatigue, headache, arthralgia, insomnia and dermatitis. Although this condition may entail a real risk of the occurrence of adverse reactions following exposure to many substances, often inhaled, or the taking of drugs, medical/scientific literature provides only a little information regarding the safest course of action to be taken when patients affected by MCS need to undergo anesthesia. It is for this reason that an electronic search of existing literature has been made, using PubMed and Scopus as a primary source, in order to find articles about patients affected by MCS and who have undergone anesthesia. The time frame considered was January 2000–December 2022. The research showed only 13 articles that dealt with anesthesia in patients with multiple chemical sensitivity in the years in question. Only 6 works, all case reports, describe the drugs used to perform anesthesia. Five cases were for general anesthesia and one was a case of subarachnoid block. No major complications related to anesthesiological practice were reported in any of the cases. The limited data does not enable the identification of anesthesiological practice and anesthetic drugs that can be used more safely in MCS patients, but the absence of serious adverse reactions in the case reports described, and in the literature in general, is reasonably reassuring about the possibility of anesthesia in MCS patients without causing serious complications by implementing easily achievable measures.

Keywords

Anesthesia; Idiopathic environmental intolerance; Multiple chemical sensitivities

1. Introduction

In 1987, Dr. MR Cullen made use of the definition of "Multiple Chemical Sensitivity" (MCS) for the first time to indicate an "acquired disorder characterised by recurrent symptoms, affecting multiple organs and systems, which arises in response to the demonstrable exposure to chemicals, even at much lower concentrations than those likely to cause ailments in the general population" [1].

In the literature, MCS is described by different pseudonyms such as idiopathic environmental intolerance (IEI), environmental illness (EI), chemical intolerance (CI) or toxicant-induced loss of tolerance (TILT), which either focus on the symptoms (IEI, EI, CI) or the pathogenetic mechanisms (TILT). In the current work, the term MCS will be used for historical and inclusive purposes, in accord with "Italian Expert Consensus on Clinical and Therapeutic Management of Multiple Chemical Sensitivity (MCS)", published in 2021 [2].

Although this is not uncommon, considering that MCS has an estimated prevalence of 0.5–6.5% in medically evaluated patients [3, 4] and according to other estimates it could even affect 12.6% of the US population [5], affecting twice as many women as men [6], many aspects of this pathological condition are still subject to discussion and definition, with regard to the aetiology, the triggers, the symptoms presented and any underlying psychological substrate.

In this regard, it should be noted that research on the possible psychological or psychiatric pathogenesis of MCS has been significantly clarified by the researchers at John Hopkins, who found the use personality tests like the MMP2 (Minnesota Multiphasic Personality Inventory 2) ineffective for the study of the pathogenesis of environmental diseases, such as multiple chemical sensitivity or fibromyalgia [7–9], concluding that the presence of psychological-psychiatric symptoms in patients with multiple chemical sensitivity (MCS), especially anxiety and depression, is compatible with the objective limitations imposed by the disease, rather than being the cause of it [10].

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Various hypotheses on the etiopathogenesis of MCS were considered: immunological mechanisms; biochemical mechanisms; vascular mechanisms; neurophysiological and respiratory mechanisms. The clinical features of MCS involve many organs and systems: neurological apparatus, otorhinolaryngological apparatus, cardiovascular and respiratory system, gastroenterological apparatus, connective and musculoskeletal tissue [2].

Recent studies have included MCS in the set of "Central Nervous System Sensitisation Syndromes", which is also referred to fibromyalgia, and Chronic Fatigue Syndrome, conditions that occur in comorbidity with MCS, as well as the Sick Building Syndrome [11–14].

Adverse reactions to drugs, foods, vapours, and environmental chemicals are a feature of MCS, and the clinical manifestations are usually symptoms rather than signs [10].

Various scientific studies also report a significant number of comorbidities, including intolerance to strong odours, which is a prevalent symptom of MCS, and the risk of chronic cardio-respiratory diseases, thereby detecting the possible coexistence of multiple pathologies in MCS patients, with obvious implications in terms of public health [15–19].

In spite of this, MCS is a relatively common condition and may entail a real risk of the occurrence of adverse reactions following exposure to many substances, often inhaled, or the taking of drugs, medical/scientific literature provides only a little information regarding the safest anesthesiological practice to be taken when patients affected by MCS need to undergo surgery [20, 21].

In this article we want to build a narrative, beginning with studies in literature, of the published data concerning the type of anesthesia practiced on patients suffering from MCS, the drugs used, the possible onset of side effects, the severity of thereof, their treatment and/or prevention, while trying to outline the allegedly safer anesthesiological practice in these patients.

2. Methods

This review was based on an electronic search of existing literature, using PubMed and Scopus as primary sources to find articles about MCS patients who have undergone anesthesia. The keywords used for the research were: anesthesia, idiopathic environmental intolerance; multiple chemical sensitivities. The time frame considered was January 2000–December 2022.

3. Results

The research showed only 13 articles that dealt with anesthesia in patients with Multiple Chemical Sensitivity (Table 1). Nine cases concern case reports [20–28].

Two of the case reports describe hypnosis as the only anesthetic used when undergoing surgery, in one case for the removal of a skin tumour and in the other for dental extraction [24, 28]. In two other articles, the authors express considerations related to the use of hypnosis as anesthesia, in response to the case report described by Facco E *et al.* [29, 30]. Another article describes a cohort of 27 patients with history of MCS, Chronic Fatigue Syndrome (CFS), or both, subjected anesthesia, without going into the details of the drugs used.

The description of anesthetic drugs used to perform anesthesia in patients with MCS is therefore reported in just 6 publications (Table 2); in two cases, totally intravenous (TIVA) anesthesia was used, deliberately avoiding the use of inhaled anesthetic, considered potentially harmful [21, 27]; in three cases inhalation anesthetics were also used: sevoflurane in two patients [20, 26] and Xenon in one patient [23]. The case report by Lorenzo Lopez M. *et al.* [25], describes the execution of the subarachnoid block, employing hyperbaric bupivacaine as a local anesthetic for a caesarean section in a patient suffering from MCS.

Fentanyl is the most widely used opioid analgesic, having been administered in 5 patients [20, 21, 23, 26, 27], while remifentanil was used in just a single case [21].

Propofol was used as a hypno-inducing drug in 3 patients [21, 23, 27], while in 1 case general anesthesia was induced with midazolam [20]. General anesthesia was performed without the use of curare in two cases [23, 26], while Rocuronium was used in two patients [21, 27] and cisatracurium in one patient [20]. Resolution of neuromuscular blockade with sugammadex was described in just one patient [21].

Acetaminophen was used for post-operative pain in 2 patients [20, 21], in one case in association with Bubrenorphine [20]. Morphine was used in one patient [27]. In two patients, local anesthesia was carried out for analgesia: in one case with lidocaine added with epinephrine [21], in the other with ropivacaine [27].

No immediate complications related to anesthesiological practice were reported in any of the cases.

4. Discussion and Conclusions

Multiple chemical sensitivity is a relatively unknown syndrome, characterised by adverse effects occurring following exposure to low levels of chemical substances. It includes a variety of symptoms such as muscular weakness, migratory joint pains, psychological disturbances (such as anxiety and depression), respiratory distress (including chronic bronchitis and asthma), auto-immune disorders, and gastro-intestinal and genito-urinary tract dysfunction [31–33].

Specific measures must be adopted when patients with MCS require hospitalisation, to avoid the onset or deterioration of symptoms [6, 34].

The need for surgery and, therefore, anesthesia, leads to further potential problems due to the operating room environment and above all the use of drugs and materials necessary for the execution of scheduled surgeries in patients who may develop adverse effects when exposed to these substances [6, 21].

The most relevant problems for anesthesia appear to be adverse drug responses and prolonged depressed consciousness, postoperative hypotension, nausea and vomiting, fatigue, reduced cognitive ability and adverse drug reactions. The duration of reactions to anesthesia appears to range from <1 hour to >7 days [6, 31].

Most of these reactions seem manageable or preventable with appropriate measures that will need to be adapted to the sensitivity of the individual patient. In accordance with

TABLE 1. Articles discussing anesthesia in patients with MCS (January 2000–December 2022).

	Year	First Author	Title	Language	Scopus	PubMed
1	2000	Maberly J, [22]	Multiple chemical sensitivity: phased initiation by anaesthetics and new building	English	×	
2	2008	Fisher MM, [31]	Anaesthesia for patients with idiopathic environmental intolerance and chronic fatigue syndrome	English	×	×
3	2011	Stoppe C, [23]	Xenon anaesthesia for laparoscopic cholecystectomy in a patient with multiple chemical sensitivity	English	×	×
4	2013	Piroli A, [20]	Anaesthesia management in patients with multiple chemical sensitivity syndrome	English	×	×
5	2013	Facco E, [24]	Hypnosis as sole anaesthesia for skin tumour removal in a patient with multiple chemical sensitivity	English	×	×
6	2013	Pullman M, [29]	Comfortably numb	English	×	×
7	2013	Castelnuovo G, [30]	Good communication and outcome after anaesthesia	English	×	×
8	2014	Lorenzo López M, [25]	Elective cesarean section in a patient with MCS syndrome	Spanish	×	×
9	2015	Gibson PR, [6]	Unmet health care needs for persons with environmental sensitivity	English	×	
10	2018	Fernández Martin MT, [26]	Sevoflurane anaesthesia for nasal surgery in a patient with multiple chemical sensitivity	English Spanish		×
11	2019	Esnaola Iriarte B, [27]	Anesthetic management of hysterectomy and double adnexectomy for borderline left ovarian tumor in a patient with MCS syndrome	Spanish	×	
12	2019	Sato Boku A, [21]	General anesthetic management of a patient with MCS for oral surgery: a case report	English		×
13	2020	Cozzolino M, [28]	Hypnosis as sole anesthesia for dental removal in a patient with MCS	English	×	×

MCS, Multiple Chemical Sensitivity.

the data in the literature [20, 21, 31, 34], some of the main recommendations to follow in the treatment of these patients are:

- hospitalisation in a single room, with the door closed;
- avoiding exposure to substances that the patient reports as harmful;
- preparing a latex-free hospitalisation environment and the operating room;
- scheduling top-of-the-list surgery;
- performing careful pre-operative pharmacological history and avoiding the administration of drugs to which the patient reports having had adverse reactions.

On the other hand, there would not seem to be any benefit in performing pre-operative skin testing for drug allergies, due to conflicting results and which, in any case, are not useful to defining the outcome [31].

This research showed only 13 articles that dealt with anesthesia in patients with Multiple Chemical Sensitivity (Table 1).

Some of these articles do not, however, contain information on the type of anesthesia and/or drugs used, which is not very useful to defining the best anesthesialogical practice in these patients.

The article by Malberly J and Anthony H [22], for example, describes the case of an allergic woman who developed MCS after receiving anesthesia, considering it a probable joint cause. Fisher MM and Rose M [31] make an interesting analysis of the data in the literature, providing a series of useful recommendations for the safe and balanced management of anesthesia in these patients, but without providing specific information on the drugs used. The article by Gibson PR *et al.* [6], even if it does not specifically describe the anesthetic drugs administered, is interesting because it describes

TABLE 2. Articles describing drugs used for anesthesia in patients with MCS (January 2000–December 2022.

	Year	First author	Title	-Type of intervention -Type of anaesthesia -Used drugs
1	2011	Stoppe C, [23]	Xenon anaesthesia for laparoscopic cholecystectomy in a patient with multiple chemical sensitivity	-Laparoscopic cholecystectomy -General Anaesthesia -Xenon-Fentanyl-Propofol
2	2013	Piroli A, [20]	Anaesthesia management in patients with multiple chemical sensitivity syndrome	-Laparoscopic cholecystectomy -General Anaesthesia -Hydrocortisone sodium -Succinate-chlorphenamine maleate (premedication) -Fentanyl-Midazolam-Cisatracurium-Sevofluorane -P.O. A: Acetaminophen-Buprenorphine
3	2014	Lorenzo Lopez M, [25]	Elective cesarean section in a patient with MCS syndrome	-Cesarean Section -Subarachnoid block -Hyperbaric bupivacaine
4	2018	Fernández Martin MT, [26]	Sevoflurane anaesthesia for nasal surgery in a patient with multiple chemical sensitivity	-Nasal Surgery -General Anaesthesia -Sevoforane-Fentanyl
5	2019	Esnaola Iriarte B, [27]	Anesthetic management of hysterectomy and double adnexectomy for borderline left ovarian tumor in a patient with MCS syndrome	-Hysterectomy and double adnexectomy -General Anaesthesia -Midazolam-Clorfenamina-Desametasone + Ranitidine (premedication) -TIVA: Propofol-Fentanyl-Rocuronium -P.O. A: TAP block with ropivacaine + morphine i.v.
6	2019	Sato Boku A, [21]	General anesthetic management of a patient with MCS for oral surgery: a case report	-Oral Surgery -General Anaesthesia -TIVA:Propofol-Fentanyl-Remifentanil-Rocuronium -L. A.: Lidocaine+Epinephrine -Decurarization: Sugammadex -P.O. A: Acetaminophen

P.O. A, Postoperative Analgesia; L. A, Local Anesthesia; MCS, Multiple Chemical Sensitivity; TIVA, Total Intra-Venous Anesthesia.

the experience of 179 environmentally sensitive patients who had received general anesthesia prior to surgery: 51% had been anesthetised using only intravenous anesthesia, 28% had received both intravenous and inhaled anesthesia, 6.0% had been anesthetised using only inhaled anesthesia and 19% did not know which type had been used. 54% of those who received general anesthetic referred to having had a long-term negative reaction; the most common were nausea and vomiting, fatigue and reduced cognitive capacity. More rarely, more severe reactions such as difficulty breathing, depression, heart problems, palpitations or seizures were also reported. Several participants also reported that their sensitivity had developed or worsened as a result of the anesthesia received, identifying general anesthesia as a significant risk factor in the onset or aggravation of symptoms [6].

There are, therefore, only a few studies in literature which describe the anesthesiological practice, the drugs used and any adverse reactions that occurred in patients suffering from MCS, and these are case reports in most cases (Table 2).

However, as already pointed out by Fisher M McD and Rose M in 2008, no serious adverse reactions are documented in patients with MCS subjected to anesthesia during induction, maintenance and awakening [31]. In the postoperative period, some patients reported the onset of symptoms related to anesthesia, the most common of which were nausea, vomiting, fatigue and reduced cognitive ability, which could last several days [6].

These symptoms, while understandably uncomfortable for patients, have never been life-threatening.

The publications examined in this study, although very small in number, also describe the use of general intravenous anesthetics as well as inhalers, curare, benzodiazepines, local anesthetics and analgesics in patients with MCS, without the onset of severe adverse reactions.

The limited available data does not enable the identification of anesthesiological practice and anesthetic drugs that can be used safely in MCS patients, but the absence of serious adverse reactions in the case reports described, and in the literature in general, is reasonably reassuring with regard the possibility of subjecting MCS patients to anesthesia without causing

serious complications, by implementing easily achievable personalised measures. Further research is needed to better define the pathophysiology of MCS, any adverse reactions caused by drugs used for anesthesia and safer anesthetics, in order to ensure MCS patients have a safe perioperative pathway.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

APi—performed the research and wrote the manuscript. AC, APa, IM, EP and FM—contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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