Occupational Exposure to Halogenated Anaesthetic Gases in Hospitals

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Objective During the induction of gaseous anaesthesia, waste anaesthetic gases (WAGs) can be released into workplace air. Occupational exposure to high levels of halogenated WAGs may lead to adverse health effects; hence, it is important to measure WAGs concentration levels to perform risk assessment and for health protection purposes.

waste anaesthetic gases | hospital staff | inhaled anaesthetics | monitoring techniques | occupational risk assessment | risk control

1. Introduction

The advent of modern general anaesthesia is undoubtedly one of the most important achievements of medicine because it allows safe performance of complex surgical and diagnostic procedures [1]. Nowadays, the most commonly used anaesthetic gases are halogenated gases, i.e., sevoflurane ($C_4H_3F_7O$; CAS: 28523-86-6; 1 ppm = 8.17 mg/m^3 at 1 atm and 25 °C), isoflurane ($C_3H_2ClF_5O$; CAS: 26675-46-7; 1 ppm = 7.52 mg/m^3 at 1 atm and 25 °C) and desflurane ($C_3H_2F_6O$; CAS: 57041-67-5; 1 ppm = 6.87 mg/m^3 at 1 atm and 25 °C) [2]. These chemicals appear initially in a liquid form and after being vaporized, volatile anaesthetics are administered via inhalation in a carrier gas (e.g., oxygen), alone or as a mixture (e.g., through mechanical ventilation, endotracheal tube, laryngeal mask airway, face mask, etc.). However, a certain amount of gases, known also as waste anaesthetic gases (WAGs), could be released or leak out and spread in the workplace (i.e., operating rooms, dental clinics and veterinary settings), thus giving rise to potential occupational exposure [3]. The emission of these gases in the atmospheres of operating rooms can be ascribed to various causes. The anaesthetic techniques used for the induction and/or maintenance of anaesthesia may play a fundamental role [4][5]. Exposure levels may depend on the type of mask worn by patients during anaesthesia [6]. In particular, face masks are frequently used in the treatment of paediatric patients and in this context a relevant release of anaesthetic gases from the face mask can be observed due to lack of cooperation of the patient [7][8][9][10][11][12]. However, even in the case of patient intubation, gas releases may occur during the medical procedures. In fact, the anaesthetic gases can be released from leaks in the anaesthesia system (e.g., from tubing, seals, gaskets, etc.) [13]. WAGs can also escape from around the patient's endotracheal tube or laryngeal mask airway if the cuff is not properly inflated or the wrong size is used [14].

Other factors that could be related to exposure to WAGs are poor efficiency of the air removal/WAGs scavenging systems and of the room ventilation system [15][16][17][18]. Furthermore, improper anaesthetizing techniques and inappropriate behaviours can favour the release of WAGs. These include, for example, improperly connected tubes and fittings for the anaesthesia machine, turning on the anaesthetic gas before the scavenging system is active, not turning the gas off when the mask is removed from the patient's face or removing the mask too quickly before the system has been flushed and the use of incorrect procedures for filling refillable vaporizers [11][13]. Finally, even during the patient's extubating, there may be a release of anaesthetic gas from the patient respiratory system or from the apparatus [19].

Despite the constant search for safer anaesthetic methods, nowadays occupational exposure to anaesthetic gases still represents a significant risk within hospitals [20][21][22].

Anaesthetists, nurses, surgeons and other members of the medical personnel are professionally exposed to anaesthetic gases depending on work practices [23]: operating room personnel are generally more exposed than the personnel of other hospital wards. Further, a stratification of the occupational risk was hypothesized for healthcare professionals conventionally present in the operating room, according to the different level of exposure, with a higher risk for anaesthetists, a lower risk for surgeons and an intermediate risk level for the remaining nursing staff [12][21].

Many safety and health authorities and institutions, such as the U.K. Health and Safety Executive in the framework of the COSHH (Control of Substances Hazardous to Health) regulation, require the routine monitoring of WAGs concentrations in operating rooms to assess occupational exposure. This can be done by environmental and/or biological monitoring. Environmental monitoring is the most standardized way to assess exposures to WAGs and to determine the compliance with occupational limit values, while biological monitoring assumes importance because it provides additional information on the body burden of anaesthetic gases and early effects. However, the occupational exposure to WAGs can be measured through the use of different environmental monitoring techniques, following more or less complex monitoring protocols, during different types of operating sessions and with respect to various temporal resolutions [8][20][24][25][26].

2. Occupational Exposure to Halogenated Anaesthetic Gases in Hospitals

2.1. Halogenated WAGs and Concentrations Time Trends

In addition to being well-known chemical risk factors, halogenated WAGs are key and current stressors of climate change. The fact that desflurane, which has the highest global warming potential among WAGs, is less used than isoflurane and sevoflurane is in line with climate-smart anaesthesia care procedures. The reason behind the increasing use of sevoflurane should be sought in the different pharmacokinetic and toxicodynamic properties of halogenated anaesthetic gases. While patients recovering from anaesthesia feel less confused when desflurane is used, sevoflurane is useful when rapid inhaled induction of anaesthesia is needed [27]. Sevoflurane is also

characterized by a low solubility in blood, allowing more precision in the control of anaesthesia and a rapid induction to awakening, an advantage in paediatric anaesthesia and general recovery from anaesthesia [28][29].

The retrieved mean concentrations were segregated by decades and analysed. The median (max, min) of these values was calculated and depicted in **Figure 1**. This figure shows an increase of the sevoflurane concentrations in the 2000s and a raise in the median for isoflurane in the 2010s. Likewise, desflurane also shows an increase over the past decade.

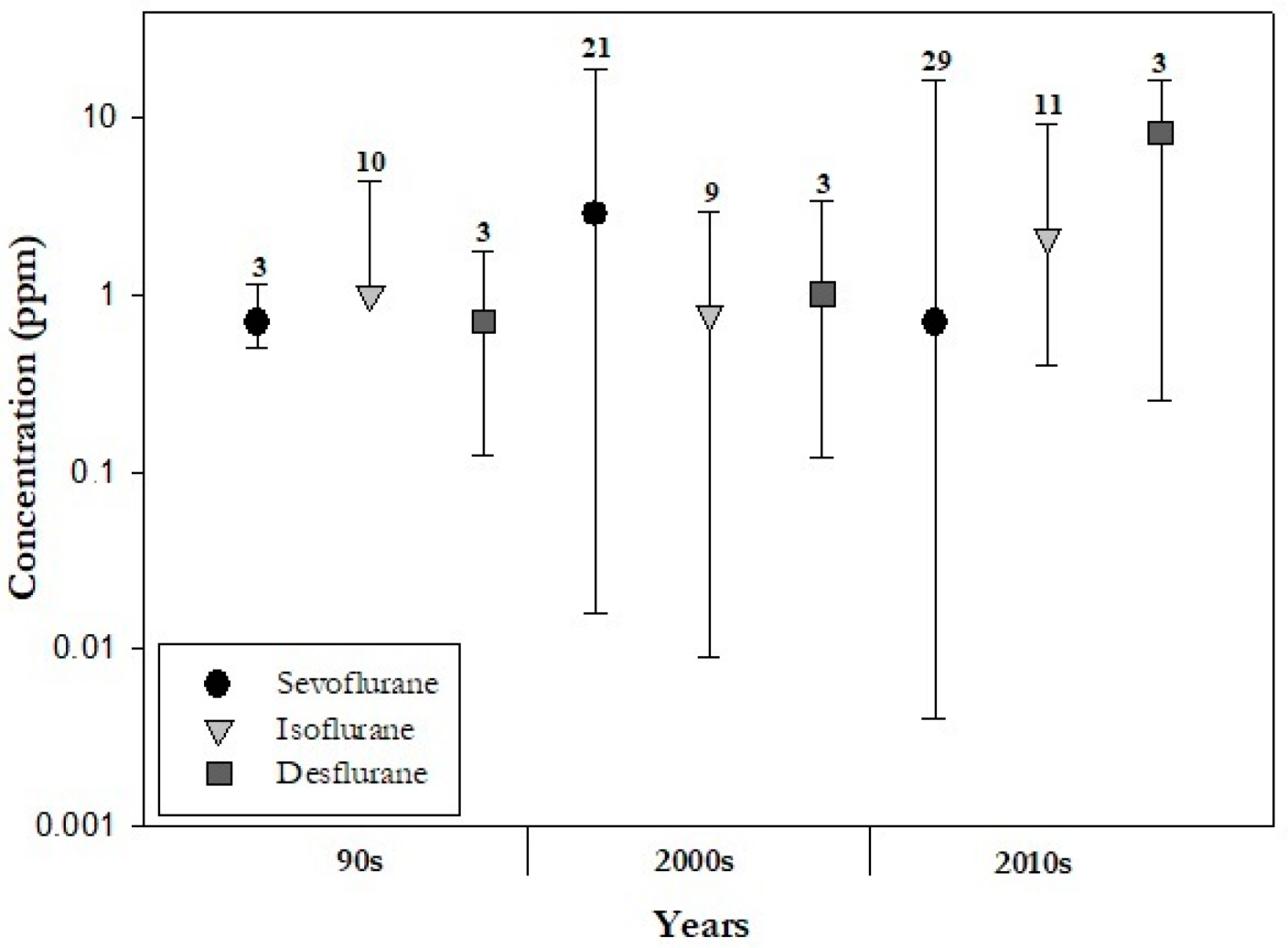

Figure 1. Median (circle, triangle and square), maximum and minimum (error bars) values of sevoflurane, isoflurane and desflurane concentrations in the 1990s, 2000s, 2010s, and number of studies considered per anaesthetic gas.

2.1.2. Air contamination by WAGs in Different Hospital Areas

Overall, in the operating rooms, higher mean values were measured (up to 19 ppm) with respect to the other investigated environments. In a few articles [30][31][32], the environmental monitoring was performed in anaesthesia rooms (excluded from **Figure 2** due to the low number of available data). These are separate premises adjacent to operating theatres, used for the induction of anaesthesia in the UK. This is not the case in the other countries (i.e.,

US, Canada, Australia and most Scandinavian countries), where anaesthetic induction typically takes place in the operating room [33].

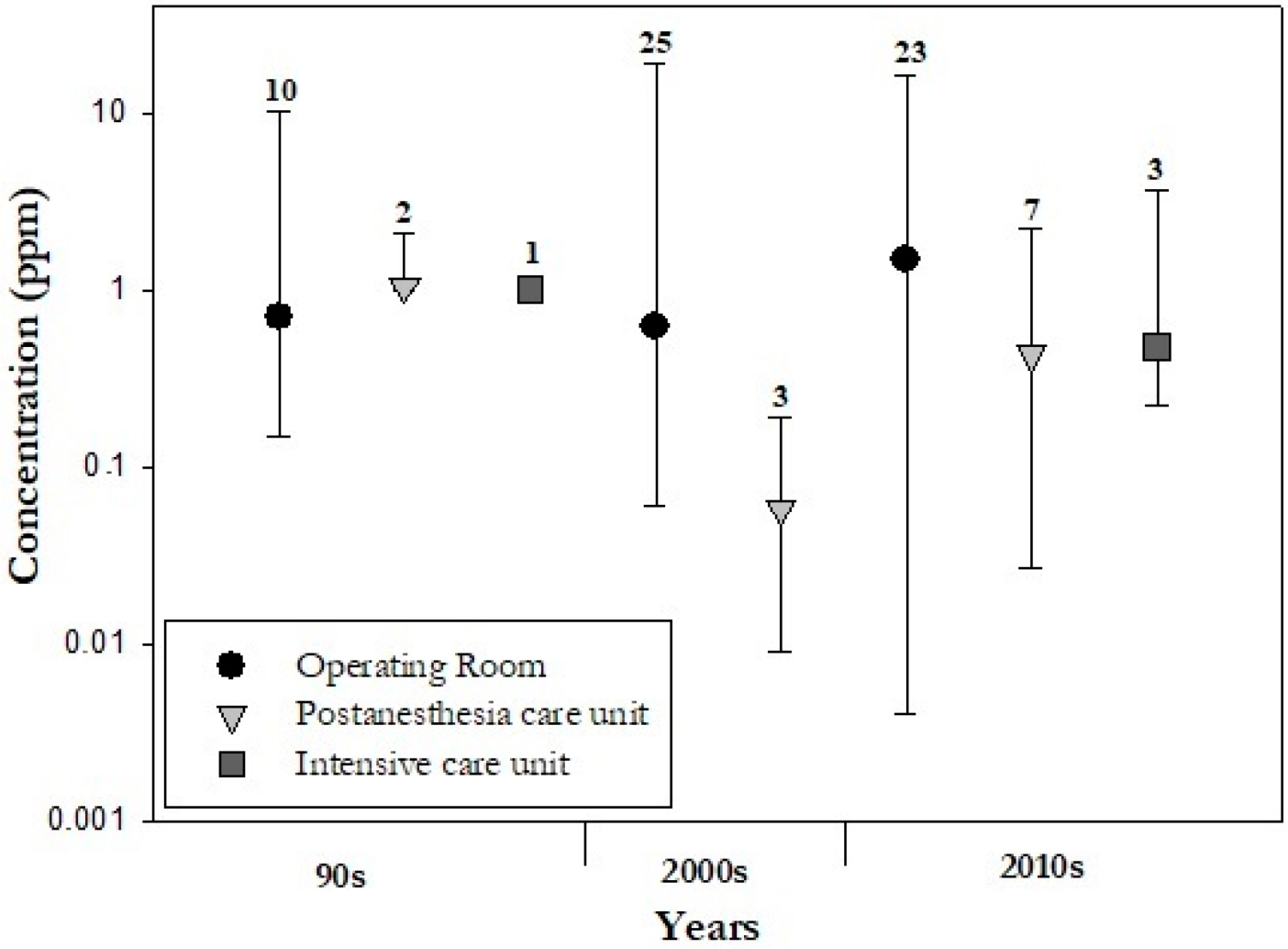

Figure 2. Median (circle, triangle and square), maximum and minimum (error bars) values of all three gases concentrations (sevoflurane, isoflurane and desflurane) in the operating room, post-anesthesia and intensive care units, respectively. Divided in decades (1990s, 2000s, 2010s), number of studies considered per different hospital areas are shown.

2.1.2. Mitigation of WAGs emissions

WAGs emissions can be mitigated by means of scavenging systems, i.e. devices directly connected to the anaesthetic equipment or placed near the patient that take the gases released from the machine and direct them out of the operating room. A picture of the average efficacy of scavenging systems in reducing WAGs air concentrations is shown in **Figure 3**.

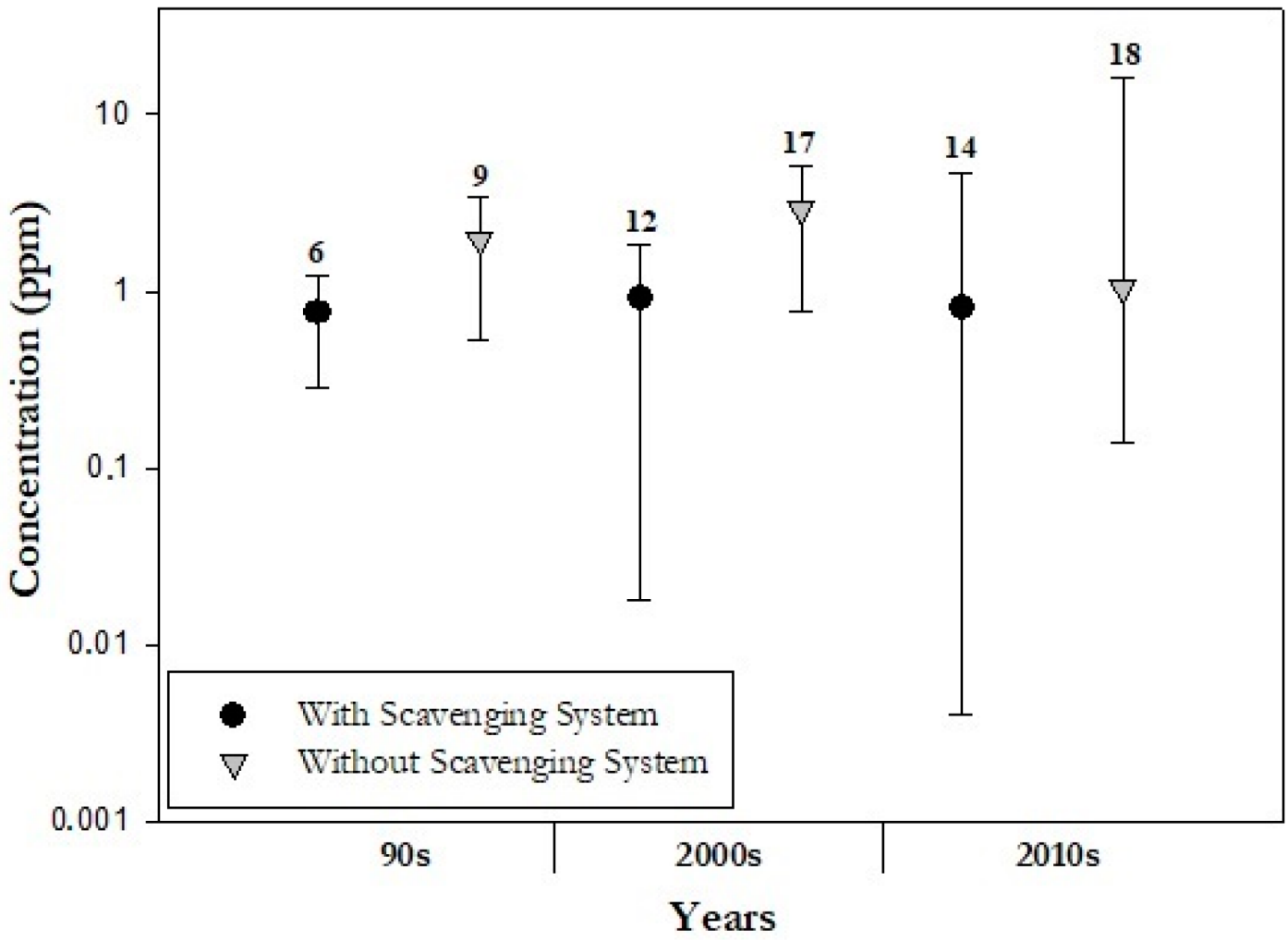

Figure 3. Median (circle and triangle), maximum and minimum (error bars) values of halogenated gases (sevoflurane + isoflurane + desflurane) measured with and without scavenging systems. Results are presented per decade (1990s, 2000s, 2010s). The number of studies considered is also shown.

As shown in the **Figure 3**, there was always an increase in median concentrations when the scavenging system was not used, especially during the 1990s and 2000s.

Furthermore, the maxima are also greater for the mean concentrations obtained without using a scavenging system. WAGs scavenging system is the primary line of defence against exposure; however, a properly designed heating, ventilation and air conditioning (HVAC) system can also help contribute to the dilution and removal of WAGs not collected by the scavenging system or escaping from leaks in the anaesthesia equipment or even resulting from poor work practices. Therefore, the efficiency of a scavenging system on the mitigation of exposures to anaesthetic gases appears to be appreciable.

2.2. Types and Evolution in Monitoring Techniques

Several techniques and approaches were used to investigate exposures or air contamination from halogenated gases. The monitoring techniques applied can be divided into real-time and time-integrated techniques (**Figure 4**).

The first instruments allow a simultaneous sampling and an analysis at high temporal resolution while time-integrated techniques provide an average sampling time data.

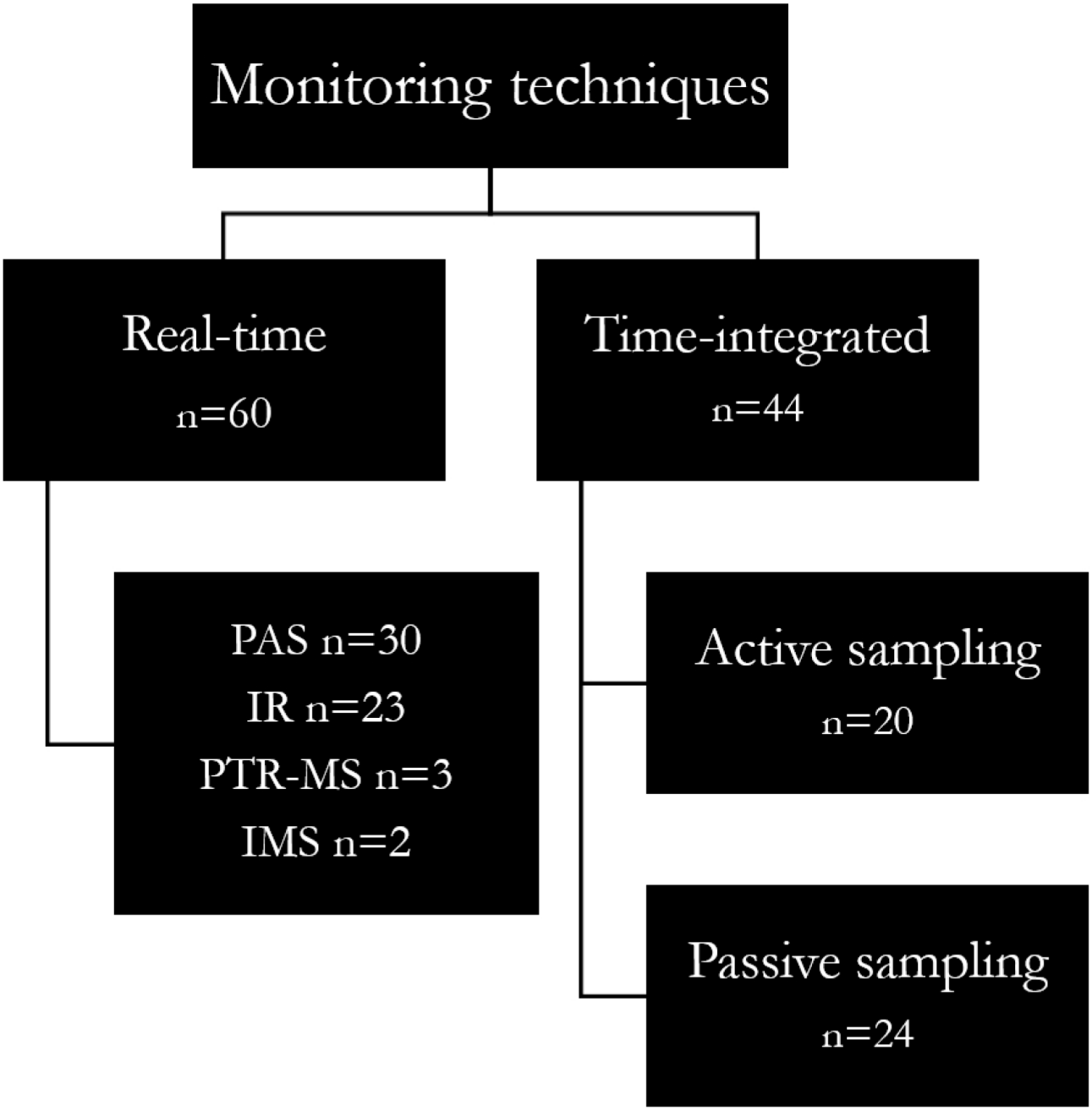

Figure 4. Block Diagram of monitoring approaches for anaesthetic gases. PAS = photoacoustic spectroscopy; IR = infrared spectrophotometry; PTR-MS = proton-transfer-reaction mass spectrometry; IMS = ion mobility spectrometer.

2.2.1. Real-Time Monitoring

A detailed analysis of monitoring methods used for the sampling of WAGs in hospital settings revealed that the real–time approach is predominant (58% of the papers). Using these techniques, the identification of short-term

transient peaks and an immediate exposure assessment became also possible. These instruments are essential to detect leak sources and control unacceptable exposures, and thus for a real-time management based on exposure data [34]. Since the NIOSH REL (2 ppm, 60 min) is currently in use although not specific and based according to the lowest level analytically detectable in the 1970s, it may be useful to adopt a real-time approach to assess short-term exposures. Furthermore, given the recent use of a combination of different gases to achieve optimal anaesthesia, the use of selective direct reading monitors can be crucial for a selective measurement of all the anaesthetic gases in the air mixture.

The most used real-time technique (**Figure 4**) is the photoacoustic spectroscopy (PAS) (51% of cases), mostly because of its solidness and user-friendliness [35]. The photoacoustic unit can be also connected to a multipoint sampler to obtain nearly simultaneous information from different areas of surgical units. As for other real-time approaches, a sample pre-treatment before measurement is not required. The resolution is in the order of 0.01 ppm, and the sampling interval is in the order of 60 s. However, PAS monitors are affected by some limitations. Among these, the sampling interval of PAS systems is usually quite large and dependent on the number of multi-point sampling locations and simultaneous monitoring of other gases [36]. So, it is possible that the staff is actually exposed to higher gas concentrations at some time-points not detected by the gas monitor (for details see [37]). Moreover, temperature, changes in ambient pressure, air humidity and the compresence of other gases and vapours such as N_2O and alcohols may produce interference signal during monitoring [38]. The PAS is not suitable for personal sampling as it cannot be worn by the staff and placing tubing in the breathing zone of individuals would greatly affect their work activities, which can be particularly sensitive for healthcare workers. However, it appeared that PAS was used for personal sampling in most of the cases (90%), using tubes fixed on the health care personnel and connected to the photoacoustic monitor [4].

Single-beam infrared spectrophotometry (IR) is also widely used (40%) for the real-time monitoring of gases, probably for its rapidity to provide results: the estimated time resolution from a routine sample varies from seconds to a few minutes. As for PAS systems, the IR monitor mostly used (i.e., the MIRAN SapphIRe series (Thermo Electron Corporation, Waltham, MA)) weights about 10 kg, which is incompatible with personal monitoring. The measurement range is up to 30 ppm for halogenated agents and the detection limit varies according to the model, but in general it ranges between 0.01 and 0.2 ppm. Fourier transform infrared spectroscopy (FT-IR) devices (e.g., the GASMET DX-4030 (Gasmet Technologies (UK) Ltd.)) are more complex and powerful compared to the IR analysers discussed above because they can analyse all frequencies simultaneously and allow an analysis with a detection limit of 0.1 ppm [39].

Other real-time techniques can be used for real-time WAGs monitoring, such as the proton-transfer-reaction mass spectrometry (PTR-MS) and ion mobility spectrometry (IMS).

2.2.2. Time-Integrated Sampling

In a considerable part of the selected articles (39%), anaesthetic gas concentrations were collected through time-integrated approaches allowing the collection of information about the average concentration throughout an entire

work shift (about 8 h), which is well-suited for long-term exposure assessment. In such a case, sampling methods can be classified as active (44%) or passive (56%).

In general, active sampling of anaesthetic gases is performed using sorbent tubes packed with a suitable material (e.g., Anasorb 747, XAD-2 or ORBO-33) and connected to a low-flow sampling pump. Direct air sampling using collection containers (e.g., the FKV Bottle-Vac) or Nalophan bags was also used in a few cases. Active sampling works by means of a pump which, connected to the sample collector, sucks the air that passes through the absorber for WAGs collection.

Passive or diffusive sampling requires a longer sampling time than the active sampling to collect the same amount of analyte, but is characterized by ease of use and cheapness [40][41]. Specifically, the SKC VOC-Check, 3M 3500, Draeger Orsa 5, Zambelli TK200 and ISC Maugeri Radiello® were used. Furthermore, diffusive sampling is particularly suitable for use in the operating room because of its very small size [21]. The sampling time varies upon the sampler type, the chemical of interest and the expected concentrations, for instance from less than 1 h to some weeks.

Either active or passive sampling implies sample collection onto collection media, which must be subsequently analysed in a laboratory, typically by gas chromatography after chemical or thermal desorption.

Chemical desorption is usually carried out with carbon disulfide. Instead, thermal desorption is a two-stage process occurring at high temperatures (100–300 °C) and using cold traps as refocusing devices. Desorption is followed by capillary gas chromatography, with mass spectrometric of flame ionization detection [42][43][44][45]. These approaches allow us to obtain the most reliable long-term exposure data for testing compliance with 8 h time-weighted average occupational exposure limit values (e.g., TLV–TWAs). Available studies outlined that gas chromatography is generally used for sample analysis (95%). However, in a few cases, samples collected in reservoir bags were analysed by infrared spectrometry [31][46].

2.2.3. Real-Time vs. Time-Integrated Monitoring

In recent years, there has been an increasing use of real-time analysers (PAS and IR monitors) compared to time-integrated approaches (active and passive sampling), probably because these techniques allow immediate feedback of exposure levels as well as the identification of the work phases and practices most at risk, also making possible an immediate adjustment of incorrect risk management practices [47].

In fact, more and more portable real-time instruments have been developed and are now available on the market, which allows the acquisition of the best dataset for short-term exposure assessment (peak exposures). As an example, portable gas chromatographs can be regarded as promising techniques for real-time monitoring of gas at fixed positions in the environment [48]. This method can quantify the air concentrations of anaesthetic agents offering a simultaneous, selective and continuous monitoring of several different halogenated gases in a single analytical run. These instruments also offer modular arrangements so that various detectors can be used. The most sensitive monitor is based on mass spectrometry (GC-MS), which delivers lab-quality results in minutes.

It is worth noting that, in some cases, time-integrated and real-time approaches were combined [31][49][50], using a diffusive or active sampling for personal monitoring and a real-time monitor placed in a fixed position to measure air contamination in different operating rooms or also in different areas of the same one. In particular, real-time approaches (e.g., photoacoustic spectroscopy, ion mobility spectroscopy, infrared spectroscopy, portable gas chromatography (GC)) can be useful to investigate exposure profiles and to identify exposure peaks, which is crucial to assess short-term exposures by comparison with short-term exposure limits [51]. However, the real-time methods are generally less reliable (in terms of accuracy, sensitivity, precision and specificity to the chemical/variable of interest) if compared to reference-grade methods [52]. Overall, real-time methods are being successfully used complementary to reference monitoring, but they are not yet validated as alternative techniques for reference instruments. On the other hand, time-integrated measurements, typically based on diffusive or active sampling and following GC analysis, are recommended for a robust determination of 8 h averaged exposures and can be very useful for the a posteriori correction of real-time data to achieve better accuracy.

3. Conclusions

In conclusion, despite the observation that environmental monitoring is dominant, it may be useful to combine it with biomonitoring to get a complete picture for risk assessment purposes, including biomarkers of early effects. For this reason, it would be very important to identify valid biomarkers of exposure to complement environmental monitoring information to be used in the practice of occupational hygiene. Furthermore, since sevoflurane is increasingly used in anaesthetic practice, it is important to derive health-based limit values for sevoflurane capable of protecting workers from acute and chronic effects. Real-time techniques are mostly used with sampling intervals consistent with the considered limit value (e.g., the NIOSH REL, 60 min). However, it can be also useful to measure the WAGs by a real-time analysis combined with a contextual time-integrated monitoring to improve accuracy and obtain the most reliable data for testing the compliance with 8 h occupational exposure limit values (e.g., TLV–TWAs) as well as for risk management purposes. As a general rule, it is very important to know in detail the uncertainty of exposure measurements and/or some analytical figures of merit such as the analytical specificity, precision and accuracy for a reliable identification of exposure events/patterns and for a sound quantification of health risks [53].

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