MAYO CLIN PROC. 2000;75:273-277 © 2000 MAYO FOUNDATION FOR MEDICAL EDUCATION AND RESEARCH

Subspecialty Clinics: Anesthesiology

Occupational Exposure to Trace Concentrations of Waste Anesthetic Gases

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Abstract

The relationship between exposure to trace concentrations of waste anesthetic gases in the operating room and the possible development of adverse health effects has concerned health care professionals for numerous years. Results of studies have been conflicting. In the late 1960s and early 1970s, some US and European epidemiological studies of operating room personnel showed an increase in the incidence of adverse health effects, including spontaneous abortion and development of congenital abnormalities in offspring. However, subsequent analysis of these studies by 2 independent groups showed that the apparent increase in adverse health effects was most likely due to flaws in these studies' methods and data collection. A later prospective study showed no causal relationship between exposure to trace concentrations of waste anesthetic gases and adverse health effects. Each institution should have a waste anesthetic gas management program that includes scavenging of waste anesthetic gases, work practices to reduce contamination, documented maintenance and regular checking of all equipment, and education of all personnel on this subject. A mechanism for reporting work-related health problems should be in place in each institution.

Mayo Clin Proc. 2000;75:273-277

ASA=American Society of Anesthesiologists; NIOSH=National Institute for Occupational Safety and Health; OSHA=Occupational Safety and Health Administration; PACU=postanesthesia care unit

Trace concentrations of waste anesthetic gases have been implicated as a cause of various adverse health effects in personnel in the operating room. Early reports were anecdotal, but in 1967 Vaisman[1] published data from the Soviet Union suggesting that fatigue, exhaustion, and headache occurred frequently in anesthesiologists and that female anesthesiologists had an increased risk of spontaneous abortion. That same year, Fink et al[2] published data from animal studies showing that the embryos of rats exposed to high concentrations of nitrous oxide had an increased incidence of skeletal abnormalities. During the next decade, other similar reports were published.[3-5] More recently, after an epidemiological analysis of these articles by 2 independent groups[6,7] and a prospective study,[8,9] the consensus is that no data show any risk of adverse health effects to personnel in medical units where waste anesthetic gases are scavenged. To understand the means by which this conclusion was reached, it is necessary to review the work on toxicity of anesthetic agents in animals as well as the results and analysis of the human epidemiological studies performed in several countries.

TOXICITY OF INHALED ANESTHETIC AGENTS IN ANIMALS

Several studies have been designed to demonstrate toxicity of volatile anesthetics in animals. Experiments to show the development of mutagenicity, carcinogenicity, organ toxicity, and adverse reproductive or developmental effects in animals have been described. None of the currently used inhaled volatile anesthetic agents, halothane, isoflurane, enflurane, sevoflurane, and desflurane, have been shown to cause severe adverse effects with clinical or trace exposure levels, either in the short or long term. In certain settings, nitrous oxide has been shown to cause adverse effects in animals (see section on reproductive effects).

MUTAGENICITY

The inhalational agents currently used have been tested for mutagenicity in both bacterial and mammalian cell systems.[10-14] The conclusion is that these agents have no mutagenic potential, and the results of most tests of DNA damage have been negative. Fluroxene and trichloroethylene, which are no longer used, are mutagens. Despite the negative results with currently used agents, reports on analyses of body fluids and blood from operating room personnel, eg, sister chromatid analyses,[11,15-18] continue to give conflicting results and are difficult to interpret because other factors in the operating room environment, such as exposure to radiation, other drugs, and aerosol sprays, may be involved.

CARCINOGENICITY

Many carcinogenic studies have been done in rodents.[12,19-24] Chloroform and trichloroethylene were found to be carcinogenic in rodents given large doses by oral lavage,[25,26] although this method of administration is not relevant to operating room personnel. Modern inhaled agents (isoflurane, halothane, enflurane, methoxyflurane, and nitrous oxide) were administered on several days for many weeks, often for more than a year, and tested on mammals for development of mutagens and carcinogens.[19,23] Both gross and microscopic examinations of the animals were performed, and no evidence of development of any cancer was found. The newer volatile agents,[14] sevoflurane and desflurane, have not undergone formal testing but were approved for clinical use by the Food and Drug Administration presumably because of the lack of carcinogenicity associated with the group of inhaled agents currently in use.

ORGAN TOXICITY

Long-term studies of chronic exposure to the inhaled anesthetic agents, halothane, isoflurane, enflurane, and nitrous oxide, have shown little evidence of major pathologic conditions developing in the kidneys, liver, gonads, or other organs.[27-30] Organ toxicity is not attributed to the direct effect of the drug per se but to the metabolites produced by cytochrome P-450–mediated biotransformations. Both hepatotoxicity and nephrotoxicity may occur because of generation of toxic metabolites in the target organ. Chloroform causes centrizonal hepatic necrosis with fatty infiltration of the liver and kidneys and renal tubular necrosis. Halothane can cause a minor degree of reversible liver damage with abnormal liver function test results. Nephrotoxicity may occur because of the metabolic liberation of inorganic fluoride, eg, with methoxyflurane. Sevoflurane and its metabolites are not directly hepatotoxic and were studied after reports of development of nephrotoxicity when low gas flows of anesthetic were used. A degradation product of sevoflurane, formed in the presence of soda lime, compound A, a vinyl ether, was implicated, but there have been no further reports that this has any clinical importance.[31] Halothane hepatitis develops as a result of a definite mechanism, the immune sensitization to a halothane-induced antigen specific to patients with halothane hepatitis, not because of chronic exposure to halothane.[27,32]

REPRODUCTIVE EFFECTS

There have been numerous investigations of anesthetic effects on the reproductive process in animals involving mating behavior, fertility, embryonic and fetal wastage, development of congenital abnormalities, and postnatal behavior and survival. This process has been reviewed in detail,[33] and, although not all agents have been tested for all reproductive indices, results indicate that only nitrous oxide has adverse reproductive effects. Nitrous oxide in concentrations greater than 50% is teratogenic, causing an increased incidence of fetal resorption and visceral and skeletal abnormalities, when administered to pregnant rats for 24-hour periods during organ development and when given in low concentration (0.1%) continuously to rats during pregnancy.[34,35] These experimental conditions are not encountered by any personnel in the operating room. Other inhalational agents, halothane, enflurane, and isoflurane, have been shown to be teratogenic in rodents when administered at anesthetic concentrations for several hours during pregnancy.[33,36,37] These effects may be caused by the physiological changes associated with these anesthetic agents, rather than by the agents themselves. The manufacturers of sevoflurane and desflurane have studied teratogenic effects of these agents and have reported no reproductive toxicity.

EPIDEMIOLOGICAL STUDIES IN HUMANS

Since Vaisman's study in 1967,[1] which examined the health of operating room personnel, trace levels of anesthetic gases have been suspected to affect the health of operating room personnel adversely. Subsequently, many reports from the United States and Europe were published. In a 1970 study of operating room nurses in Denmark, Askrog and Harvald[3] reported an increase in the incidence of spontaneous abortion or premature neonates. In the United States, Cohen et al[4] surveyed operating room nurses and anesthetists in 1971 and found an increased incidence of spontaneous abortion. In 1972, Knill-Jones et al[5] surveyed female physicians and found an increase in the frequency of the development of congenital abnormalities in offspring, an increase in spontaneous abortion, and involuntary infertility in British anaesthetists. Consequently, the American Society of Anesthesiologists (ASA) Ad Hoc Committee on Adverse Reactions to Anesthetic Agents met in June 1972 with members of the National Institute for Occupational Safety and Health (NIOSH), and the ASA National Health Survey of Operating Room Personnel was initiated.[38] This retrospective survey published in 1974 showed that female personnel working in the operating room had an increased risk of spontaneous abortion, congenital abnormalities in their children, cancer, and hepatic and renal disease. These data and those from animal research resulted in an NIOSH recommendation that waste anesthetic gases be scavenged in all areas. A second national survey was planned to begin in 1978 to determine whether scavenging waste anesthetic gases would lead to a reduction in the reported problems, supporting the inference that waste anesthetic gases had caused the problem. However, in 1977, without performing the follow-up study, NIOSH recommended that standards for waste anesthetic gases be established.[39] The recommended exposure level for

nitrous oxide, measured as a time-weighted average, was 25 ppm during anesthetic administration, and the permissible exposure level for volatile agents was 2 ppm. The Occupational Safety and Health Administration (OSHA), the federal enforcement agency for occupational safety and health, also developed technical instructions concerning waste anesthetic gases[40] but never officially promulgated the standards.

In the 1980s, investigations questioning the conclusions of the early epidemiological studies began to appear. In 1985, Buring et al,[6] at the request of the ASA, analyzed the 17 published studies that examined outcomes after exposure to trace anesthetic gases. They estimated the overall relative risks of various adverse health effects developing in operating room personnel from the 6 studies with similar populations, exposures, and endpoints. The relative risk was calculated as the ratio of the rate of disease among those exposed to the comparable number among those not exposed, to 95% confidence limits. They reported that the most consistent adverse finding (ie, data from more than 1 or 2 studies) was an increase in the rate of spontaneous abortion in pregnant operating room personnel. However, these investigators noted that all the studies had flaws: there was no quantified level of exposure, and there was a lack of confirmation and verification of reported adverse outcomes as well as a lack of information on many possible confounding variables. Responder bias due to both the wording of the survey and the respondents' answers could not be excluded. The positive results of the analysis could be attributed to bias and uncontrolled confounding variables, such as occupational stress, and exposure to other contaminants including blood and aerosol sprays. They recommended that a prospective study be performed. That same year, Tannenbaum and Goldberg[7] independently reviewed the relevant epidemiological literature and reached a similar conclusion. In another important study, Axelsson and Rylander[41] showed how epidemiological data examining spontaneous abortion are inaccurate when outcome data are not verified. Using Finnish National Health Registry data, they demonstrated that the statistical differences between exposed and control patients were eliminated completely when medical records of all patients were examined. More recently, Spence[8] and Maran et al,[9] using annual questionnaires, prospectively surveyed all British female medical school graduates age 40 years or younger working in hospitals during the years 1977 to 1984. Their analyses showed that female anesthesiologists had no increased risk of infertility. In addition, there was no association between the incidence of spontaneous abortion or the development of congenital abnormalities and possible risk factors such as occupation of the mother, hours in the operating room environment, and use of scavenging equipment. Recently, Axelsson et al[42] reported that night work, shift work, and staff shortages among Swedish midwives were associated with an increased incidence of late spontaneous abortions, whereas the use of nitrous oxide as an analgesic for labor and delivery was not.

In contrast, in dental offices, Rowland et al[43,44] reported reduced fertility and increased risk of spontaneous abortion among female dental assistants exposed to nitrous oxide in areas where nitrous oxide was delivered without scavenging systems, but not in areas where scavenging systems were used. In dental offices where anesthetic gases are not scavenged and there is no ventilation system, nitrous oxide levels may exceed 1000 ppm, much higher than levels reported in operating rooms or in postanesthesia care units (PACUs).[39] The American Dental Association, in its Guidelines for the Use of Conscious Sedation, Deep Sedation and General Anesthesia in Dentistry, recommends the use of scavenging systems to capture waste gases when anesthetic gases are used for analgesia and anesthesia.

In summary, no studies have demonstrated that trace concentrations of waste anesthetic gases adversely affect personnel in operating rooms or PACUs where scavenging systems are used.

SCAVENGING OF WASTE ANESTHETIC GASES AND VENTILATION SYSTEMS

All anesthesia machines have a scavenging system to capture waste anesthetic gases. These gases are then vented to the outside air, either passively or actively by a dedicated suction system. These systems should be checked with each use and maintained regularly by trained technicians. The American Institute of Architects, in its 1992 Guidelines for Construction and Equipment of Hospitals and Medical Facilities, established recommendations for ventilation systems in operating rooms (15-21 air exchanges per hour, of which 3 must be fresh outside air) and in PACUs (6 air exchanges per hour, of which 2 must be fresh outside air).

The 1977 NIOSH document[39] recommended scavenging of waste anesthetic gases, work practices to reduce contamination, monitoring of trace anesthetic gases, and medical surveillance of personnel. These recommendations were never promulgated by OSHA as a statute. Recently, OSHA revised its manual *Waste Anesthetic Gases: Workplace Exposure*. This document, which will be published on the OSHA Web page (http://www.osha.gov/), recommends that institutions have a waste anesthetic gas management program that includes scavenging of waste gases, work practices to minimize exposure, and monitoring of trace gases. When nitrous oxide is the sole anesthetic agent, OSHA[40] recommends that no worker be exposed to 8-hour time-weighted average concentrations greater than 25 ppm during anesthetic administration. In addition, no worker should be exposed to concentrations of halogenated anesthetic agents greater than 2 ppm for a period not to exceed 1 hour. Because no data support the development of adverse health effects after exposure to trace anesthetic gases, OSHA has changed the requirement for medical surveillance to a recommendation for a preplacement medical examination. Each institution should also provide a system whereby an employee can report a work-related health problem.

Exposure limits vary among countries. Denmark, Italy, Norway, Sweden, and the United Kingdom have set exposure limits for nitrous oxide at 100 ppm, and the Netherlands, like the United States, has set them at 25 ppm. The differences illustrate the difficulty in setting standards without adequate data since exposure to trace concentrations of waste anesthetic gases has not been shown to cause adverse health effects to personnel working in operating rooms in which scavenger systems are being used.

CONCLUSION

Neither animal nor epidemiological studies have proved that adverse effects develop after a person is exposed to trace levels of waste anesthetic gases. Indeed, the analyses by Buring et al[6] and Tannenbaum and Goldberg[7] of the reports of adverse effects after exposure to waste anesthetic gases and the study by Axelsson and Rylander[41] showed that inaccurate study design can give misleading results in an epidemiological investigation, especially one that has confounding variables and nonresponders. In the only prospective study, which was carried out by Spence[8] and Maran et al[9] over several years, no causal relationship was shown between exposure to waste anesthetic gases with or without scavenging systems in the operating room and adverse health effects in personnel. The 2 studies from dental offices where there was no scavenging of waste anesthetic gases showed increased infertility and spontaneous abortion.[43,44] However, the conditions in which these personnel worked with excessively high levels of nitrous oxide are not similar to those found in an operating room where levels higher than 25 ppm are uncommon.

Scavenging of waste anesthetic gases is recommended for all areas, and work practices to reduce contamination should be established. In addition, there should be a program for management of waste anesthetic gases, with a documented maintenance schedule for all anesthesia machines and the ventilation system in the operating room and PACU. Moreover, an educational program is necessary for all personnel working in these areas, which includes an overview of the topic, with information on maintenance and checking procedures of all anesthetic and scavenging equipment as well as work practices available to reduce contamination. Studies have shown that, with these procedures, trace anesthetic gases in the operating room[45] and PACU[46] can be maintained below the levels recommended by NIOSH and OSHA.

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