Reproductive Outcomes among Dental Personnel: A Review of Selected Exposures

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ABSTRACT

Since the late 1960s, investigators have assessed the risks associated with exposure to a variety of potentially harmful agents used in dental practice. This paper provides a brief overview of the epidemiologic literature examining the associations between occupational exposures to elemental mercury and anesthetic gases and reproductive outcomes, such as spontaneous abortion, congenital abnormalities and reduced fertility. Most of the epidemiologic evidence points to a significant relationship between exposure to nitrous oxide and both spontaneous abortion and reduced fertility. There is also evidence for an association between exposure to ethylene oxide and spontaneous abortion, but on the basis of the limited research available, this relationship does not appear to be statistically significant. At this time, evidence of a relationship between exposure to elemental mercury and spontaneous abortion, congenital abnormalities and reduced fertility is limited. Good mercury hygiene by dental personnel and the use of scavenging equipment on nitrous oxide systems and exhaust systems on ethylene oxide sterilizers may reduce the risk of adverse reproductive outcomes.

MeSH Key Words: abnormalities/epidemiology; dentists, women; pregnancy outcome

Since the late 1960s, investigators have assessed the risks associated with exposure to a variety of potentially harmful agents used in dental practice.[1] Most of this research has focused on mercury and nitrous oxide (N_2O), but sterilizing agents such as ethylene oxide (EtO) have been examined briefly as well. In particular, epidemiologic researchers have investigated the effects of these agents on reproductive outcomes such as spontaneous abortion, congenital abnormalities and reduced fertility. This report provides a brief overview of the epidemiologic literature examining these associations.

Common Exposures in the Dental Office

Mercury

The major sources of mercury contamination in humans are occupational exposure to mercury and the consumption of mercury-rich foods, particularly fish.[2] Because mercury is finely dispersed in silver amalgam, most dental personnel are exposed to this element daily, particularly the vapour of elemental mercury.[3] In this review, only elemental mercury is discussed. Mercury is readily absorbed into the body through the skin during handling and by inhalation. About 80% of inhaled vapour is absorbed into the blood, where the dissolved vapour can remain long enough to cross the blood–brain barrier; from the brain, it is oxidized and slowly eliminated.[2–5] Elemental mercury also moves readily from the placenta to the fetus.[5] Mercury has a relatively high vapour pressure, is monoatomic in nature and has high lipid solubility, all properties that contribute to its toxic effects.[5]

Mercury appears to affect pregnancy outcome, causing problems such as spontaneous

abortion and congenital abnormalities.[2] It exerts its toxic effects on the central nervous system of the developing fetus,[6] as well as the central nervous system, kidneys and skin of adult humans.[2,6,7] Overexposure to mercury may cause weakness, fatigue, anorexia, headache, loss of memory, drowsiness or insomnia, and tremors in the hands, lips, head, tongue or jaw.[2,7–10] Studies have shown that workers exposed to mercury also experience problems with digestion, eyesight and the urinary system.[2,7–11] Other symptoms include irrational behaviour, excitability, inability to concentrate, indecisiveness and depression.[2,8,12]

The American Conference of Governmental Industrial Hygienists (ACGIH) develops guidelines for safe levels of exposure to toxic agents. ACGIH established a threshold limit value — a concentration of a substance to which most workers can be exposed without adverse effects — of 0.025 mg/m^3 as a time-weighted average for a normal 8-hour workday and a 40-hour workweek for mercury vapour.[13] In addition, the Occupational Safety and Health Administration has established a permissible exposure limit of 0.1 mg/m^3 as a ceiling limit — a legally imposed value which at no time is to be exceeded.[13] Brodsky and others[2] have suggested that as many as 10% of dental offices exceed this ceiling limit.

Nitrous Oxide

In the 1970s, several studies linked occupational exposure to anesthetic gases with congenital malformations and spontaneous abortion.[14] Anesthetic gases slow the rate of cell division and increase the rate of abnormal cell formation and chromosomal aberrations.[14] N_2O in particular is used in dental offices, primarily as a sedative to reduce patient anxiety[14]; this compound has been shown to oxidize vitamin B_{12} and impair synthesis of methionine, folate and thiamine.[15] N_2O has also been shown to cause fetal malformations, to increase fetal deaths and to decrease litter size in laboratory animals.[16,17] Exposure to N_2O may result in short-term behavioural effects; may decrease mental performance, audiovisual ability and manual dexterity; and may cause neurologic effects, renal and liver disease, and long-term adverse reproductive effects such as spontaneous abortions and reduced fertility.[17] Although exposure to N_2O in dental operatories is small (measured in parts per million), the exposure is continuous and occurs over the long term. Investigators have suggested that, because of cumulative effects, chronic exposure may be more dangerous than short-term exposure to higher concentrations.[18]

Ethylene Oxide

EtO is a flammable, highly reactive, colourless gas used to sterilize dental equipment.[19] Acute exposures to EtO may result in eye pain and blurred vision, sore throat, respiratory irritation and lung injury, headache, nausea, dizziness, vomiting, diarrhea, shortness of breath, convulsions, skin irritation and cyanosis.[20,21] Chronic effects include mutagenic changes, neurotoxicity, peripheral paralysis, muscle weakness and cancer.[20,21] The chronic effects of EtO exposure would be of most concern to dental personnel, as workers are regularly exposed to trace amounts of EtO, which would accumulate over their working lifetime. EtO has been shown to affect a number of reproductive outcomes in laboratory animals; however, there is little epidemiologic data on its reproductive effects on humans.[19]

Reproductive Outcomes

Spontaneous Abortion

Spontaneous abortion generally refers to a pregnancy ending in the spontaneous loss of the embryo or fetus before 20 weeks of gestation.[2] Spontaneous abortion has been linked to increasing maternal age, smoking, alcohol consumption, use of coffee, history of previous spontaneous abortion, parity and gravidity.[22] In the first study to draw attention to an association between anesthetic gases and spontaneous abortion, Vaisman[1] reported in 1967 that 18 of 31 pregnancies among Russian female anesthetists ended in spontaneous abortion; only 7 pregnancies had no complications. Five years later, one of the earliest large-scale epidemiologic studies examining this relationship was published.[23] The investigators surveyed female anesthetists in the United Kingdom and reported a significantly greater frequency of spontaneous abortion among anesthetists (18.2%) than among control subjects (14.7%).

Realizing that occupational exposure to anesthetic gases may also occur in the dental professions, a number of researchers began to investigate these populations. In the United Kingdom, responses to a postal questionnaire received from 1,615 female dentists examined the relationship between occupational hazards and pregnancy outcome.[24] Among 2,291 pregnancies reported by these dentists, there was a significantly greater rate of spontaneous abortion relative to controls (12.8% vs. 10.9%). The control population, taken from a study conducted by Knill-Jones and others[25] consisted of 7,296 pregnancies among the wives of male doctors in the United Kingdom, also surveyed by mail. Both the dentists and their wives in the control population had not been exposed to anesthetic gases. The study also revealed that 13 (5.4%) of the pregnancies among working dentists but none of the pregnancies among nonworking dentists ended in spontaneous abortion after 20 weeks. Cohen and others[26] studied over 20,000 female dental assistants in the United States. The rate of spontaneous abortion was 1.7 to 2.3 times greater for female dental assistants who were exposed to anesthetic gases in the year before conception than for those who were not exposed. In

addition, there appeared to be a dose–response relationship between exposure and spontaneous abortion.

Although the majority of research in this area has reported an association between N_2O exposure and spontaneous abortion, some studies have not duplicated these results. In a cross-sectional study of hospital employees exposed to anesthetic gases, there was no statistically significant difference in rates of miscarriage among exposed employees (12.4%) and unexposed workers (9.1%), when age and smoking habits were taken into consideration.[27] The investigators suggested that the lack of significant results was due to the small number of pregnancies included in the study. However, Heidam[28] also reported no significant effects in a postal survey of female Danish dental assistants employed in private or public dentistry.

In a study conducted in California in 1995, investigators examined 1,465 respondents whose most recent pregnancy was conceived while working full-time as a dental assistant. They reported significantly more spontaneous abortions among women who worked with N_2O for 3 or more hours per week in offices without scavenging equipment than among respondents exposed to N_2O that used scavenging equipment.[17]

IN ONE STUDY, AMONG 2,291 PREGNANCIES REPORTED BY FEMALE DENTISTS, THERE WAS A SIGNIFICANTLY GREATER RATE OF SPONTANEOUS ABORTION RELATIVE TO CONTROLS.

Although most of the research examining the association between anesthetic gases and spontaneous abortion has focused on women with occupational exposure, a few studies have looked at paternal occupational exposure, with mixed findings. A survey of health conditions among 2,798 male members of the American Society of Oral Surgeons showed a greater incidence of spontaneous abortions among the wives of exposed dentists than the wives of unexposed dentists ($p < 0.01$).[29] In their study of female dental assistants, Cohen and others[26] also examined reproductive outcomes among the wives of male dentists, reporting a 50% greater incidence of spontaneous abortion among the wives of male dentists who had heavy exposure to inhalation anesthetics during the year before conception. In contrast, in their study of anesthetists, Knill-Jones and others[25] reported no significant association between paternal exposure to anesthetic gases and spontaneous abortion.

Rowland and others[19] studied 1,320 dental assistants working in California whose most recent pregnancy was conceived while working full-time. After controlling for smoking, age, lack of scavenging of N_2O and high amalgam use, the investigators found that women exposed to EtO were twice as likely as unexposed dental assistants to have any of the 3 adverse pregnancy outcomes (spontaneous abortion, preterm birth or post-term birth). However, the statistically insignificant result (95% CI = 0.7–5.7) may reflect the small number of women with self-reported exposure to EtO (n = 32). Research with other occupational groups, such as hospital sterilization staff, nurses and chemical workers, has suggested that exposure to EtO increases the risk of adverse reproductive outcomes.[30]

Congenital Abnormalities

Cohen and others[26] reported a 1.4- to 1.6-fold greater rate of congenital abnormalities among the children of female dental assistants exposed to anesthetic gases. These results were consistent with an earlier study, in which there was a significantly higher incidence of congenital abnormalities among children born to anesthetists who worked during pregnancy than among the children of those who did not work during pregnancy (6.5% vs. 2.5%).[23] In contrast, Nixon and others[26] reported that the frequency of "minor" and "major" abnormalities among children of working female dentists did not differ significantly from the frequency among children of nonworking female dentists. Others have reported no significant association between occupational exposure to mercury and congenital abnormalities in the offspring of female dental assistants.[2,6]

In a study of paternal occupational exposure, investigators reported slightly higher rates of congenital abnormalities among the wives of exposed dentists than among the wives of unexposed dentists.[29] Congenital abnormalities were reported 15% more often among the offspring of exposed dentists than the offspring of unexposed dentists, although the sample size was small and the result was not statistically significant. However, in a 1980 study by the same investigators,[26] exposure of male dentists to N_2O was not associated with a significantly greater frequency of congenital abnormalities. Brodsky and others[2] found no statistically significant association between mercury and congenital abnormalities.

Infertility

It has been suggested that exposure to N_2O reduces fertility in rats by impairing the release of certain hormones affecting ovulation.[3,31] Exposure to mercury may also impair fertility. Mercury accumulates in the brain, pituitary and thyroid[4] and may cause irregular menstrual cycles, fewer ovulations and teratogenic effects in animals.[3,4] Human research has shown abnormalities of the menstrual cycle, such as painful menstruation, changes in bleeding patterns and changes in menstrual cycle duration among workers exposed to mercury.[4]

Rowland and others[14] investigated the effect of exposure to N_2O on the fertility of 418 female dental

assistants in California who had become pregnant during the previous 4 years. After controlling for covariates such as oral contraceptive use, frequency of intercourse, age, history of pelvic inflammatory disease and use of cigarettes, the investigators found that women exposed to high doses of N_2O (indicated by duration, i.e., 5 or more hours per week) were nearly 60% less likely to conceive during each menstrual cycle than women who were either unexposed or were exposed to lower doses of N_2O ($p < 0.003$). Rowland and others[4] examined the same female dental assistants for exposure to amalgam and reported a lower probability of conception among assistants who prepared over 30 amalgams per week and had poor mercury hygiene (e.g., hand contact with mercury, carpet in the operating laboratory, history of spills in the office, improper disposal of mercury waste) than among unexposed controls. Interestingly, dental assistants with good mercury hygiene were more fertile than unexposed controls; however, the investigators did not provide possible explanations for this result.

In a 1979 study of 1,271 married female dentists in the United Kingdom, 100 (7.9%) reported a period of infertility of at least 2 years; the cause of infertility was unknown for 64 of the women.[24] In 2003, Case[31] estimated the prevalence of infertility in Canada at about 8%. Although these proportions appear similar, Case noted that the prevalence of infertility appears to be on the rise, which suggests that the prevalence in the general population was lower in previous years. Sikorski and others[32] conducted a study of 117 pregnancies among 57 Polish women employed in dental professions. The results indicated greater rates of irregularities in the women's menstrual cycles and of reproductive failures.

No studies were found that examined the association between occupational exposure in the dental professions and male infertility. Mercury has been shown (in both animal and in vitro studies) to interfere with spermatogenesis; however, little is known about the effect of mercury on human sperm function.[33,34]

Limitations in Research

There are a number of limitations in the research conducted thus far. The majority of studies examined maternal age and smoking history as important risk factors for reproductive outcomes, but few included other confounders such as alcohol consumption,[22] history of previous spontaneous abortion,[22] gestational week at time of spontaneous abortion,[17] parity,[26] or gravidity.[22,28]

Also of concern is the way in which exposures have been measured. Most research on N_2O exposure was conducted before scavenging was widely used, and none of the studies included ambient gas sampling.[22] For research on exposure to mercury, crude definitions of exposure have been used in most studies (unexposed, low exposure or high exposure), and none of the investigators measured dose or the time during pregnancy at which the subjects were exposed.[19]

Few studies have examined only dental personnel,[17,26] and most have included nurses, anesthetists and others who may be occupationally exposed to the agents of interest.[1,5,23,27] The appropriateness of the unexposed comparison groups can also be questioned. The control groups in most studies consisted of workers from the same occupational group who were not exposed to the agent in question.[17,26,28] Few studies reported whether or not subjects conceived while employed,[17,19] and Savitz and others[34] showed that results may be biased if the unexposed comparison group consists of women not working while pregnant.

Most of the data obtained in these studies was collected by postal questionnaire.[4,14,17,19,23,24,26,29] Self-administered questionnaires are limited because they are retrospective and "involve information that is subject to misinterpretation, miscollection, and variation due to the experience and education of the respondent."[18]

Conclusions

On the basis of physiological evidence,[2,6–12,14–21] personnel working in the dental professions have reason to be concerned about exposure to mercury, N_2O and EtO. To date, the epidemiologic evidence is inconclusive regarding risks for adverse reproductive outcomes associated with mercury and EtO. There is some evidence to support a direct link between exposure to N_2O and spontaneous abortion and infertility; however, this evidence is limited. More comprehensive and rigorous studies are needed to adequately assess the hazards faced by dental personnel. Good mercury hygiene by dental personnel and use of scavenging equipment on N_2O systems and exhaust systems on EtO sterilizers contribute to minimizing exposure to these toxins. These measures may ultimately help to reduce the risk of adverse reproductive outcomes.

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