

Multiple sclerosis in nurse anaesthetists

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Background: Volatile anaesthetics are chemically related to organic solvents used in industry. Exposure to industrial solvents may increase the incidence of multiple sclerosis (MS).

Aim: To examine the risk among nurse anaesthetists of contracting MS.

Methods: Nurses with MS were identified by an appeal in the monthly magazine of the Swedish Nurse Union and a magazine of the Neurological Patients Association in Sweden. Ninety nurses with MS responded and contacted our clinic. They were given a questionnaire, which was filled in by 85 subjects; 13 of these were nurse anaesthetists. The questionnaire requested information about work tasks, exposure, diagnosis, symptoms, and year. The number of active nurse anaesthetists was estimated based on information from the National Board of Health and Welfare and The Nurse Union. Incidence data for women in the region of Gothenburg and Denmark were used as the reference to estimate the risk by calculation of the standardised incidence ratio (SIR).

Results: Eleven of the 13 nurse anaesthetists were exposed to anaesthetic gases before onset of MS. Mean duration of exposure before diagnosis was 14.4 years (range 4–27 years). Ten cases were diagnosed in the study period 1980–99, resulting in significantly increased SIRs of 2.9 and 2.8 with the Gothenburg and the Danish reference data, respectively.

Conclusion: Although based on crude data and a somewhat approximate analysis, this study provides preliminary evidence for an excess risk of MS in nurse anaesthetists. The risk may be even greater than observed, as the case ascertainment might have been incomplete because of the crude method applied. Further studies in this respect are clearly required to more definitely assess the risk.

In 1982 Amaducci and colleagues¹ reported an excess of multiple sclerosis (MS) among shoe and leather workers exposed to organic solvents in Florence. Since then, a number of articles have been published on the connection between exposure to organic solvents and MS. A meta-analysis of nine studies of MS and solvent exposure found a two fold risk ratio for MS.²

Many anaesthetics are chemically related to organic solvents, and trichloroethylene, nowadays mainly used as a degreasing agent, was formerly used as an anaesthetic. As nurse anaesthetists are exposed to agents chemically related to organic solvents, we evaluated the possible risk for nurse anaesthetists to contract MS.

METHODS

There is no nationwide MS register in Sweden. Only inpatients are registered, but most MS patients treated as outpatients. We therefore had to use the following unconventional method to identify nurse anaesthetists with MS. Ninety five per cent of all nurses are members of their union, the Swedish Association of Health Professions, according to the statistics officer of the union. Members of the union receive a union magazine (*Vårdfacket*) monthly; on two occasions in 1999 we published an appeal in the magazine for MS cases to contact our clinic. A similar appeal was also published in 1999 in *Reflex*, the magazine of the Neurological Patients Association of Sweden. Ninety subjects replied. They were sent a questionnaire, which was filled in and returned by 85 subjects, 83 of which were nurses. The questionnaire requested information about years and kind of work tasks, type of anaesthetics they had used, year of first symptoms of MS, and year of diagnosis of MS. To confirm the diagnosis of MS we asked the nurse anaesthetists for a photocopy of their medical files, which we received from all of them—that is, the occupational group we focus on here. The neurologist in our group went through the medical files and confirmed the diagnoses of MS in all cases according to the criteria of Poser and colleagues.³

Main messages

- Nurse anaesthetics are at increased risk of contracting multiple sclerosis according to this Swedish study.
- Anaesthetic gases are chemically related to organic solvents.
- Organic solvents have been associated with excess risk for MS.

Policy implications

- Control measures are needed regarding pollution of anaesthetic gases in operating rooms.
- Regular measurements of these gases are needed.
- Efficient local exhaust ventilation systems or other measures to reduce exposure to anaesthetic personnel should be installed in operating theatres that do not have this equipment.

In order to calculate the expected number of MS cases among the nurse anaesthetists, we contacted the National Board of Health and Welfare and obtained the number and age distribution of active nurse anaesthetists ($n = 2083$) for 1985. This was the last year in which the Board held statistics concerning the number of nurses in various specialties. For the latter part of the study period, The Nurse Union furnished the number ($n = 2046$) and ages of registered nurse anaesthetists in 1995.

Statistical analysis

Standardised incidence ratios (SIR)⁴ were calculated using the MS incidence rates, both from the general population of

Abbreviations: MS, multiple sclerosis; SIR, standardised incidence ratio

Table 1 Age specific incidence rates and SIR with 95% CI for multiple sclerosis in Swedish female nurse anaesthetists in 1980–99

Age group, years	Swedish nurse anaesthetists		Incidence rates of	
	Number of cases	Person-years	Gothenburg women	Danish women
20–29	0	3170	9.9	11.35
30–39	0	17860	12.26	11.77
40–49	8	12260	6.33	7.62
50–59	2	4440	3.57	2.50
20–59	10	37730	SIR = 2.9 (95% CI 1.3 to 5.3)	SIR = 2.8 (95% CI 1.3 to 5.2)

References are incidence data for women in the Gothenburg region in 1950–64 and in Denmark 1950–89. The incidence rates are expressed as cases per 10⁵ person-years. For calculations, see Hernberg.⁴

women in the Gothenburg region in Sweden and from the Danish population of women as the references.^{5,6} The Gothenburg material is the largest dataset on incidence of MS in Sweden and consists of 253 patients diagnosed as probable or definite MS in 1950–64 in a population at about 400 000 individuals. These incidence rates are the highest ever published in Sweden. Through personal communication (O Andersen) we obtained data on which the graphs presented in the article were based.⁵ For comparison we also used incidence rates from the Danish Multiple Sclerosis Registry, which includes some 10 000 probable and definite cases of MS among women collected from 1950 to 1989.⁶ Again, the underlying numbers relating to the paper⁴ were obtained through personal communication (N Koch-Henriksen).

In calculating SIRs, we first estimated approximately the person-years of the nurse anaesthetists for the age categories 20–29, 30–39, 40–49, and 50–59 years by assuming the age distribution for 1985 to be representative for the 1980s and that of 1995 for the 1990s, respectively, and then multiplied the number of subjects in each age category by 10 years in order to obtain an approximate number of person-years under observation. The expected number of MS cases by age category was then calculated by multiplying the person-years of the nurse anaesthetists by the incidence rates of the Gothenburg and the Danish material per age group. The observed number of cases was then divided by the expected number of cases as summarised over the age categories in order to obtain the SIR. Confidence limits were calculated based on Poisson distribution.

RESULTS

Thirteen nurse anaesthetists cases were identified. Seven of these were diagnosed in the 1990s, four during the 1980s, and two during the 1970s. The first symptoms of MS occurred in the 1990s in five subjects, in the 1980s in another five, and in the 1970s in the other three individuals. Two nurses were diagnosed with MS prior to exposure as nurse anaesthetists and were therefore excluded.

For the remaining 11 nurses, mean age at diagnosis was 43.5 years (range 32–54 years). Mean age at the start of symptoms was 40.6 years (range 29–54 years). Mean duration of exposure prior to diagnosis was 14.4 years (range 4–27 years). Considering exposure before the start of symptoms, mean duration was 11 years (range 2–26 years). The start of exposure occurred from 1963 to 1987, mean 1977. Of the 11 nurse anaesthetists that had been exposed to anaesthetic gases prior to diagnosis, 10 were diagnosed in 1980–99, while one was diagnosed in the 1970s. Since the mean survival probability 30 years after MS diagnosis is only 50%,⁶ we abstained from calculating incidence rates for the 1970s and restricted the incidence analysis to encompass the period 1980–99, leaving 10 cases to be included in the analysis. An almost threefold and significantly increased risk was obtained for nurse anaesthetists diagnosed during the

period 1980–99, both when using the Gothenburg and the Danish incidence rates for reference (table 1).

DISCUSSION

Although based on somewhat crude data and methodology, our study suggests an increased incidence of MS in Swedish nurse anaesthetists during 1980–99, whether the reference material involves the population from Gothenburg during 1950–64 or the Danish material during 1950–89. Although there is an incongruity in time between the material concerning the nurses and the reference data, to our knowledge there are no reference data on incidence for the 1990s. The Gothenburg material also covers a second period of time from 1974 to 1988. The incidence rate is lower in this latter period, possibly as a result of the opening up a few more neurological departments in the Gothenburg area, with subsequent difficulties in getting a complete collection of cases. We therefore preferred to use the higher incidence rates of the first period as the reference in order not to underestimate the expected number of cases. In the Danish material there is a slightly decreased incidence from 1950 to 1969 and a slight increase in the incidence from 1970 to 1989. Minor changes in temporal trends from other countries are also seen, for example in Finland,⁷ Norway,⁸ and Iceland.⁹ In spite of the somewhat crude methods that had to be applied in this study, the clearly increased SIRs found for the nurse anaesthetists can hardly depend on the time incongruities.

Neurologists had diagnosed all cases as MS in our material. All cases were definite MS. The reference materials on the other hand include both definitive and probable MS cases, thereby leading to some overestimation of the expected number of cases. The more specific diagnoses among the MS nurses, whose exposure preceded the onset of the disease, were relapsing remitting MS in seven patients, relapsing progressive in three patients, and primary progressive MS in one patient. This distribution is unremarkable according to our clinical knowledge.

As already emphasised, the method of collecting cases of MS among the nurses is somewhat unconventional. We asked all nurses suffering from MS independent of specialty to answer our appeal. As there was a reference to anaesthetics in the appeal, one would expect nurse anaesthetists to be more likely to answer than nurses of other specialties. This possibility of over reporting was eliminated by scrutinising the medical files of the nurse anaesthetists to confirm the MS diagnosis. It is likely, however, that some cases were missed, especially those nurses suffering from a severe state of MS and of course those who were deceased. This might explain the low number of MS cases announcing themselves diagnosed in the 1970s, having a long period of illness and progressed up to the year of case collection in 1999. This consideration made us limit the period to 1980–99. Two of the nurses were diagnosed

some years before exposure to anaesthetics—that is, in 1978 and 1982. Their contribution to the incidence of MS was therefore also disregarded.

Most nurses in our material had a long experience of anaesthetist work and were exposed to a wide spectrum of anaesthetics. It is therefore impossible to pinpoint any particular agent as a suspected cause for the increased risk of contracting MS. However, on the whole, the volatile anaesthetics could be classified as organic solvents. Halothane is a halogenated ethane; desflurane, enflurane, and sevoflurane are all fluorinated ethers.

Anaesthetics like halothane have been reported to cause impairment in the hepatic antioxidant defence system and to accelerate oxidation reactions in guinea pig hepatic and heart tissue^{10 11}; isoflurane¹² impairs the antioxidant defence system in guinea pig kidney. Organic solvents like trichloroethylene¹³ and ethanol¹⁴ cause lipid peroxidation by formation of free radicals in animal assays. Oxidative stress from free radicals is hypothesised to be part of a pathogenic mechanism for MS.^{15–17} Mechanisms of this kind might explain our epidemiological findings regarding the nurse anaesthetists as well as the increased risk of MS in workers exposed to organic solvents.²

In conclusion, this study provides preliminary evidence for an excess risk of MS in nurse anaesthetists, although based on crude data and a somewhat approximate analysis. As the case ascertainment might have been incomplete because of the crude method applied, the risk may be even greater than observed. Further studies based on more rigorous methods should be undertaken in countries with a larger number of nurse anaesthetists in order to more definitely assess or refute the risk indicated in this study.

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