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Critical Literature Review on Exposure Assessment Methods for Metalworking Fluids in Epidemiological Cancer Study

Donguk PARK [1), 2)]

1) Department of Environmental Health, Korea National Open University, 169 Dongsungdong, Jongroku, Seoul, Korea, 110-791
2) Occupational and Environmental Epidemiology Branch National Cancer Institute, NIH, DHHS, 6120 Executive Blvd, Rockville, MD

금속가공유 노출과 암 발생위험역학조사에서 금속가공유 노출 평가 방법에 대한 고찰

박동욱 [1), 2)]

1) 한국방송통신대학교 환경보건학과,
2) 미국국립보건위(NIH), 암연구소(NCI), 직업환경역학과(OEEB)

그 동안 많은 역학연구를 통해서 금속가공유(metalworking fluid, MWFs) 노출과 여러 조직에서 암 발생위험과의 관계를 밝혔지만, 금속가공유 종류(비수용성, 수용성, 합성, 준합성)별로 구분된 위험은 아직 완전하게 규명되지 않았다. 역학조사에서 금속가공유 노출을 대체할 수 있는 인자(surrogate)로서 정성적(qualitative), 명목적(ordinal) 혹은 준정량적인(semi-quantitative) 변수들(금속가공유에 대한 노출 유무, 노출 정도: 높음, 낮음 등, 직업 유무, 근무기간 등)을 이용하여 금속가공유 노출을 평가하였다. 이러한 노출평가방법은 기본적으로 금속가공유 노출 강도(intensity)가 고려되지 않을 뿐만 아니라 노출 분류 오류(misclassification)도 항상 존재할 수 있어 금속가공유 노출은 물론이고 종류별 위험을 밝히기 어렵다. 일부 역학연구에서 금속가공유 종류별 누적 노출양(cumulative exposure level)과 암위험과의 관계를 밝혔다. 이러한 연구결과들은 모두 금속가공유 종류별로 과거노출을 추정할 수 있는 자료(정량적인 노출평가자료, 과거 직업력, 취급했던 금속가공유 종류 등)가 잘 기록되어 있는 1개의 대규모 자동차공장에서 나온 것들이다. 따라서 금속가공유에 대한 노출자료가 부족하고 사용특성에 대한 기록이 없거나 부족한 일반 인구나 산업을 대상으로 한 역학연구에서는 금속가공유의 종류별 위험을 밝히는 것은 불가능하다. 금속가공유 종류별로 과거 노출에 대한 확률(probability)을 추정하는데 일반적으로 활용할 수 있는 노출확률 메트릭스를 개발하는 것이 필요하다.

Key Words : 금속가공유(metalworking fluid, MWF), 비수용성금속가공유(straight), 수용성금속가공유(soluble), 합성금속가공유(synthetic), 준합성금속가공유(semi-synthetic)

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† 교신저자 : Donguk PARK (169, Dongsung-dong, Jongro-ku, Seoul, Korea, 110-791
Tel : 3668-4707, E-mail : pdw545@knou.ac.kr)

Ⅰ. Introduction

Metalworking fluids (MWFs), also called cutting fluids, machining fluids, or metalworking coolants, are complex mixture that may contain petroleum products, vegetable and animal fats, organic and inorganic salts, and a variety of additives. MWFs can be grouped into four major categories: straight MWF, which are undiluted mineral and fatty oils; soluble MWF, which are water emulsions of mineral and fatty oils; synthetic MWF, which are chemical solutions of organic compounds and inorganic salts in water; and semisynthetic MWF, which are emulsions of mineral oils with water and the chemicals found in synthetics (NIOSH, 1998).

Specific formulations differ from not only fluid types, but also manufacturer to manufacturer and according to the specific purpose for which the fluid is intended. In use, fluid may change as a result of other additives being applied by the operator, by contamination from being worked, from machine and hydraulic oils, and through thermal degradation. Due to complex characteristics of MWFs, workers exposure could be different from one another, which results in different health risk even though they have the same task or operations using MWFs.

Each fluid type should be evaluated as a separate risk factor for adverse health outcomes. Many epidemiological studies to date have studied association of exposure to Maws with several cancer risks. Various exposure variables were used as proxy exposure to MWFs in these epidemiological studies. Main objective of this study is to review exposure assessment methods used in various epidemiological cancer studies and to suggest appropriate method to link cancer and exposure by MWF types. This review could be served to compare exposure assessment methods for exposure by MWF types.

Ⅱ. Materials and Methods

Searches in MEDLINE (key words; metalworking fluid, machining fluids cutting oil and cancer study and MWFs etc) and other reviews were performed. Both industry-based and population or community-based epidemiological studies to examine association between cancer risks and exposure to MWFs were reviewed. Of these, study result to examine cancer risk and exposure to fluid type

Table 1. Summary of epidemiological study to assess existence of exposure to fluid type and cancer risks (only significant associations abstracted)

Type of study	Study cancer site	RR or OR(CI) [1]	significant fluid type [2]	Ever exposed to fluid type [2]	Reference
Cohort-based	Stomach	1.2(1.0-1.5)	2	1, 2, 3	Tolbert et al. (1992)
PMR [1]	Stomach	6.2(p=0.05)	2	2	Park et al.(1988)
Cohort-based	rectal	3.2(1.6-6.2)	1	1, 2, 3	Tolbert et al. (1992)
Cohort-based	Pancreatic	1.6(1.0-2.5)	2	1, 2, 3	Tolbert et al. (1992)
Cohort-based	Laryngeal	2.0(1.3-3.0)	1	1, 2, 3	Tolbert et al. (1992)
Cohort-based	Laryngeal	1.4(1.0-2.0)	2	1, 2, 3	Tolbert et al. (1992)
Cohort-based	Lung	1.1(1.0-1.2)	2	1, 2, 3	Tolbert et al. (1992)
Cohort-based	Prostate	1.5(1.0-2.3)	1	1, 2, 3	Tolbert et al. (1992)

[1] PMR: Proportional Mortality Ratio, RR: relative risk, OR : odd ratio
[2] Fluid type; 1=straight, 2=soluble, 3=synthetic

were summarized. Assessment methods for exposure to MWFs in epidemiological study were comprehensively discussed. Significant associations between cancer risk and exposure to MWFs or fluid type were mainly summarized. Epidemiological studies that examined either scrotal cancer risk or skin cancer were excluded because significant association of exposure to straight MWFs was already confirmed.

Ⅲ. Result

There have been many epidemiological studies to examine associations between exposure to MWFs and cancer risk.

Through these study results, significant associations have been observed for several cancers of a priori interest, including of stomach(Tolbert et al., 1992; Park et al., 1998), larynx(Tolbert et al., 1992), esophagus(Sullivan et al., 1998), pancreas(Schroeder et al., 1997; Park et al., 1996; Tolbert et al., 1992), lung(Zeka et al., 2004; Bardin et al., 2005; Tolbert et al., 1992), breast(Thompson et al., 2005), prostate(Agalliu et al., 2005; Tolbert, 1992) and rectum(Malloy et al., 2007; Tolbert et al., 1992; Eisen et al., 1992). Although significant associations of some cancer risks with exposure to MWFs were observed, specific MWFs type or component causing cancer risk significantly have not been identified completely.

Although industrial hygiene expert who was blinded with respect to case-control and health outcomes assigned MWFs exposure categories qualitatively based on using industry, occupation, job title, interview etc, considerable exposure misclassification could be

Table 2. Summary of epidemiological study to assess cumulative exposure to fluid type and cancer risks

Type of study	Study cancer site	RR (CI)	significant fluid type [2)]	Cumulative exposure fluid type [1)]	Reference
Case-control	pancreatic	3.0(1.2-7.5)	3	1, 2, 3	Schroeder et al. (1997)
Case-control	lung	NS	NS	1, 2, 3	Sullivan et al.(1998)
Case-cohort	upper aerodigestive tract	1.07 (1.01-1.12)	1	1, 2, 3	Zeka et al.(2004)
Cohort-based	rectal	2.7 (1.4-5.3)	1	1, 2, 3	Elizabeth et al.(2007)
Case-control	breast	1.18 (1.02-1.35)	2	1, 2, 3	Thompson et al.(2005)
Cohort-based	prostate	1.12 (1.04-1.20)	1	1, 2, 3	Eisen et al.(2001)
Case-control	liver & biliary tract	1.2 (1.04-5.6)	NS	1, 2, 3	Bardin et al.(1997)
Case-control	esophageal	1.2-3.2	1	1, 2, 3	Eisen et al.(2001)
	rectal	1.15-3.52	1	1, 2, 3	
	skin	1.03-6.74	2	1, 2, 3	
	brain	1.05-4.11	2	1, 2, 3	
	esophageal	1.28-5.25	3	1, 2, 3	
	liver	1.14-5.08	3	1, 2, 3	
Case-control	esophageal	4.1(1.1-15.0)	3	1, 2, 3	Sullivan et al.(1998)

[1)] Fluid type; 1=straight, 2=soluble, 3=synthetic possible, because information on exposure to specific MWF classes over the period of interest lacks.

Several epidemiological studies had tried to associate cancer risks with exposure to fluid types (straight, soluble and synthetic MWFs) (Table 1). These studies used only existence (never or ever) of exposure to fluid type as surrogate of exposure to fluid types. The exposure to soluble MWFs was found to be significantly associated with stomach (Tolbert et al., 1992; Park et al., 1998), pancreatic, lung, prostate and laryngeal cancer. The exposure to straight MWFs was found to be associated with rectal, lung, bladder and prostate cancer (Tolbert et al., 1992). Silverstein et al(1988) studied mortality among bearing plant workers exposed to MWFs. To examine the exposure from operation and fluid type, exposure categories were combined by exposure to fluids types (straight and water-based MWFs) and operations (grinding, machining, assembly etc). Grinding operation using water-soluble MWFs was found to be significantly associated with the risk for stomach cancer. Also moderate evidence that exposure to straight MWF increase the risk for pancreatic cancer. Although exposure were assessed by the combination of operation and two fluid types (straight and water-soluble including soluble, semi-synthetic and synthetic), intensity was not assessed.

Tolbert et al. (1992) conducted a mortality study to examine cancer risks associated with specific fluid types in a cohort of over 30,000 workers employed at two automotive plants (Tolbert et al., 1992). Their results were based on assessment of only existence of exposure to each fluid type (ever/never) and employment duration as exposure variables. Exposure intensity over time workers exposed was not assessed, which misclassification remains likely although associations of certain fluid type with a cancer sites were observed.

There had been epidemiological studies to assess intensity of exposure to specific fluid types one automotive part manufacturing plant consisted of three plants (Table 2). They estimated cumulative exposure by fluid type in which the calendar-time-specific estimate of total mass particulate(mg/m3) in each job was weighted by the time spent in that job. On the basis of recent plant records, fluid types were assigned to each plant, department and job specific exposure category. Scale factors were estimated to express aerosol exposures relative to the baseline levels measured a specific duration. Schroeder et al (1997) had conducted nested case-control study of automotive workers (case 667, control 3,041) to associate lung cancer risk with exposure to MWF types or combination of specific MWF types (Schroeder et al., 1997). Individual estimates of exposure quantity cumulated and duration for specific classes of machining fluids were derived using complete work histories and exposure measurements. They found that OR for lung cancer among fluids type was different.

In Eisen et al (2001)'s follow-up cohort mortality study conducted in the same automobile plants, different cancer site among fluid classes assessed by cumulative exposure were also found(Eisen et al., 2001). Thus, cancer sites specific to each MWF types (straight and rectal cancer; soluble MWFs and skin, brain; synthetic and liver) were found. In particular, significant associations between skin and brain cancer risks and cumulative exposure to soluble MWFs in grinding operation were first reported to date. In addition, they reported the possible evidence that modest risk of several cancer sites (digestive, prostate and leukemia) may persist at current levels of exposure to water-based MWFs, although airborne exposures declined over the study period.

Recently, Zeka et al. (2004) re-examined aerodigestive track risk in a cohort of workers exposed to MWFs from same automotive plants, using improved case definition and more recently diagnosed cases(Zeka et al., 2004). Significant association between larynx cancer incidence and cumulative straight MWFs exposure was found, which is consistent with a Eisen et al's finding(Thompson et al., 2005). However, association of aerodigestive track risk with exposure to other MWF types was not found. The results obtained through cumulative exposure estimate to each fluid type could be more easily generalized to currently exposed workers because specific causal agents or type of MWFs could be identified. Epidemiological studies found significant associations exposure to straight MWF with rectal, lung, prostate and esophageal, soluble MWF with breast, skin and brain, and synthetic MWF with esophageal and liver cancer by assessment for quantitative cumulative exposure to fluid types (Table 1)

Ⅳ. Discussion

In National Institute for Occupational Safety and Health(NIOSH) 1997 criteria document recommending a reduced exposure limit for MWFs(NIOSH, 1998), NIOSH concluded that MWFs used before the mid-1970s were associated with cancer in several organ sites. However, NIOSH did not find difference of cancer risk or cancer sites based on types of MWFs until 1998.

Most of epidemiological studies that examined associations of exposure to MWFs with cancer risk used either qualitative exposure to MWFs or ordinal, semi-quantitative exposure to MWFs as proxy of exposure to MWFs. As MWFs exposure surrogate, an operation, industry or job handling MWFs, duration of exposure to MWFs and existence of exposure to MWFs (ever/never) without classification of fluid class was assessed. These exposure assessments basically assume that the intensity of MWFs exposure is the same for all workers holding the job handling MWFs, exposure levels have remained the same over time and the intensity of exposure is related to tenure of employment.

In epidemiological studies, the best feasible proxy of dose is usually the cumulative exposure which is the product of an estimate of the exposure level and the respective duration of exposure summed over different periods of exposure (Kauppinen, 1991). This is best done by linking job and work-area exposure data with their personal job histories from company or labor union records for the period of interest (Belletti et al., 1993). It is necessary to estimate the personal exposure-time profiles of the subjects in the epidemiological study.

The cumulative exposure was calculated as the product of the exposure measured for a certain occupational group and the time exposed. However, it may be very difficult work to construct cumulative exposure level because the provability and exposure intensity of workers handling MWFs may naturally change over time. Thus, fluid type and amount used have been highly variable over both time and operation characteristics.

If desired, quantitative exposure time profiles could be a better predictor to estimate cumulative exposure to fluid types. To estimate cumulative exposure during the period exposed, specific information such as job history including job title, department and dates that type of MWFs used and monitoring data should be available. The difficulty is compounded in the case by the changes that have occurred in the formulation of these fluids over time. Chemical inventory plant purchased over time, industrial hygiene records and interviews with plant personnel will provide the basis for assigning types of MWF by year, if any, to each plant-department-job-year combination.

Many epidemiological studies have used “ever/never employed in an MWFs using plant”, “duration of employment in an MWFs using plant or operation” and “existence of exposures to MWFs” as surrogates for exposure to MWFs, because information related to exposure to fluid types are scanty or missing.

However, these approaches are hard to differentiate the specific type of MWFs that may cause the different health risk. Major limitation of these studies is that information is not sufficient to quantitatively assess exposure to fluid types. The use of a specific MWFs type instead of wider MWFs not specified as entity of exposure is recommended because the effect may be specific to each MWF type and assigning exposure to a group of MWFs may dilute the effect unless other members of the group share the same property.

The critical issue is how to obtain this detailed information over several decades of interest in order to determine the probability and intensity of exposure to specific MWF types. Exposure probability could be estimated if types of MWF that workers were handling during a certain period were known. It is rare to find that these information are kept very well because of complexity of MWFs. It is well known that assessment of quantitative exposure levels is, ideally, more appropriate than other exposure assessment approaches, because it may more closely approximate the true measure of dose. However, MWFs exposure data during long retrospective period are few. No sufficient monitoring measurements for MWFs exposure are available for epidemiological study that had examined the association between exposure to MWFs and cancer risk until recently. In addition, information on MWFs components and type and operation that has changed over time had not been recorded well for even large plant.

Only Eisen’s team(Zeka et al., 2004; Malloy et al., 2007; Thompson et al., 2005; Eisen et al., 2001; Agalliu et al., 2005; Bardin et al., 1997; Schroeder et al., 1997) constructed cumulative MWFs exposure level that subjects had exposed over the entire period, in order to examine association between exposure to each MWF types and several cancer risk. Past exposure was retrospectively estimated relative to the measurement measured by them. Uncertainty associated with these quantitative estimates could be controlled to some extent only when specific information such as job title, operation, type of MWFs that subject were exposed over time were well recorded. It is very difficult to assess exposure to specific MWF types or components if related information lacks. The main reason that risks associated with specific fluids types have not been examined is that information to estimate probability and intensity for exposure to fluid types were not easily obtained. In a plant utilizing MWFs, it is not easy work not only to recognize complex characteristics of MWFs, but also to record changes in MWF types, components used and exposure measurement over time. Due to the complicated characteristics by MWF types, even workers handling it may unaware of not only various additives but also fluid types used. In an epidemiological study, only subject’s last full time occupations or job title recorded on death certificate may be considered. The lack of workplace exposure assessment or detailed records of specific cutting oils/fluids used over the study period limits study ability to associate more precisely a specific type of MWFs or components exposure with the elevated mortality rates for workers.

All epidemiological study to associate cancer risk with exposure to MWF types was from one large automobile plant. There has been no study that examines association between cancer risk and exposure to MWF types from other metalworking working industry including small machine shops. Characteristics of exposure of workers from small scale plant may be substantially different from the large scale plants where machine and operation workers are involved in are relatively fixed and work history relatively recorded well. Basic approach to estimate the probability and intensity for exposure to each MWF types we suggested could be applied to further epidemiological study. To date, there has been only one study to suggest the way to estimate the probability and intensity for exposure to mineral oil according to task type in metal and textile industry (Belletti et al, 1993). Exposure probabilities for other fluid types were not studied.

In case that information for retrospective assessment is either sparse or missing, a generalized approach to assess probability and exposure intensity of MWF types is necessary, which could be applied to the study that record on work history and MWF types lacks relatively.

Ⅴ. Conclusion

Although significant associations of some cancer risks with exposure to MWFs have been found through various epidemiological studies, specific MWF types causing cancer risk significantly have not been identified completely. Most of epidemiological studies used either qualitative exposure to MWFs or ordinal, semi-quantitative exposure to MWFs as proxy of exposure to MWFs. MWFs exposure intensity was not considered in these qualitative exposure assessment methods. In addition, misclassification of exposure may exist. Several epidemiological studies found significant association between cancer risks and cumulative exposure to fluid types (straight, soluble and synthetic MWF). These study results were from one large automobile plant where enough information to construct cumulative exposure to each MWF types were recorded well. A generalized assessment method to estimate probability and intensity for exposure to MWF types is needed to be developed. This exposure method could be applied to the study that record on work history and MWF types lacks relatively

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