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Original Article

A Meta-analysis of Epidemiological Studies on the Relationship between Occupational Electromagnetic Field Exposure and the Risk of Adult Leukemia

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Abstract

Since the first paper by Milham et al. suggested that occupational exposure to an electromagnetic field (EMF) could increase the risk of adult leukemia, many epidemiological studies on this problem have been published. In this report the method of meta-analysis was used to summarize the results from these papers quantitatively. The combined relative risk of all leukemia (RR=1.11), as well as acute lymphocytic leukemia (RR=1.38), acute myeloid leukemia (RR=1.07) and chronic lymphocytic leukemia (RR=1.14) increased but not significantly. So far, it is difficult to make a consistent conclusion about the relationship of the occupational exposure to EMF and adult leukemia. Further carefully designed case-control and cohort studies using the more valid means of exposure assessment are required.

Key words: electromagnetic field, leukemia, occupational exposure, meta-analysis

Introduction

The National Institute of Environmental Health Science (NIEHS) of America held a scientific conference on the health effects of electromagnetic field exposure from June 16th to 24th, 1998. It was suggested that there was some possible association (GROUP 2Bi Possibly according to the International Agency for Research on Cancer (IARC)) between the residential or occupational exposure to an extremely low frequency electromagnetic field and the risk of leukemia among children and adults according to the results of a number of studies during past two decades, especially of the various epidemiological studies on this issue. Concern about a possible association between cancer and electric and magnetic fields from generation and use of electricity was first suggested in the study of childhood cancer by Wertheimer and Leeper [1]. A weak association was suggested by the first epidemiological paper on occupational electromagnetic exposure and the risk of leukemia among electrical workers [2]. Since then, nearly one hundred epidemiological studies of both occupational and environmental exposure have been published. No, or only weak, correlation was found by most of the studies on the leukemia risk from occupational exposure to an electromagnetic field. Until now it has been difficult to make a consistent conclusion from these studies directly. In this paper we conducted a quantitative meta-analysis of epidemiological studies on the relationship between occupational exposure to electromagnetic field and the risk of adult leukemia.

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Method

To prepare this paper, all epidemiological studies published from the first paper by Milham et al.[2] from the period of 1982 through December 1998 that examined occupational electromagnetic field exposure and the risk of adult leukemia were collected through a literature search using MEDLINE®. Their references, as well as citations from electric and magnetic field newsletters and any other sources, were cross-checked and additional papers were added to the list. Relative risk was used as a measure of the relationship between occupational exposure to electromagnetic field and the risk of adult leukemia. For case-control studies, the odds ratio was used as a surrogate measure of the corresponding relative risk. The overall log(RR) was estimated as

$$\text{Log(RR)} = \Sigma (w_i \times \log(RR_i)) \div \Sigma w_i$$

Where w_i is a weight that consists of the reciprocal of the variance of the $\log(RR_i)$[3]. The homogeneity of $\log(RR_i)$ across the k studies was tested by using Woolf's χ^2 statistic[4]:

$$\chi^2 = \Sigma w_i [\log(RR_i)-\log(RR)]^2, \text{ with df=k-1}$$

The variance of the natural logarithm was derived from the confidence interval provided in the study or was calculated by

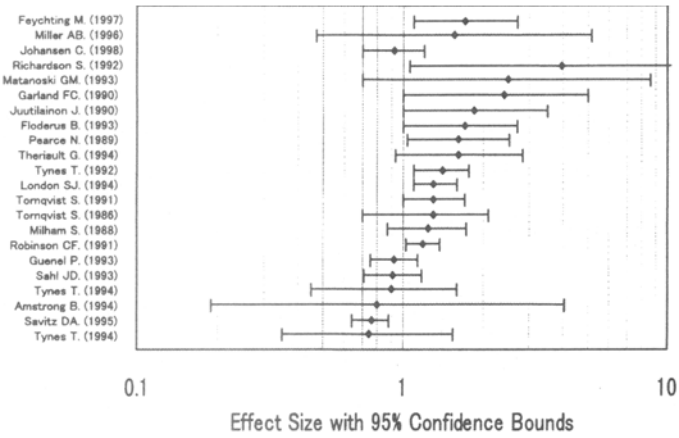

Fig. 1 Epidemiological studies on occupational EMF exposure and adult all leukemia

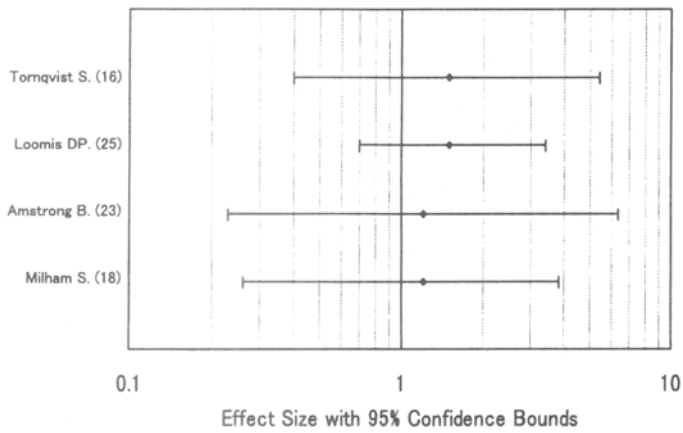

Fig. 2 Epidemiological studies on occupational EMF exposure and adult acute lymphocytic leukemia

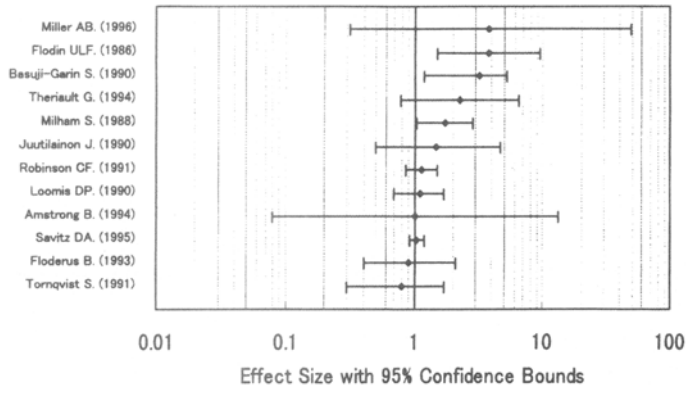

Fig. 3 Epidemiological studies on occupational EMF exposure and adult acute myeloid leukemia

means of standard formulas [4]. A two-tailed P value of less than 0.05 was considered to indicate statistical significance. We used both a fixed-effects model and a random-effects model to calculate the pooled relative risk [5]. If all the relative risks of the results were examined to be homogeneous among various studies, the fixed-effects model was used to get the combined effect of the all studies. However, the random-effects model was used as alternative method for estimating the combined effect of heterogeneous studies [6]. The meta-analysis was conducted with EPIMETA software developed by the Center for Disease Control

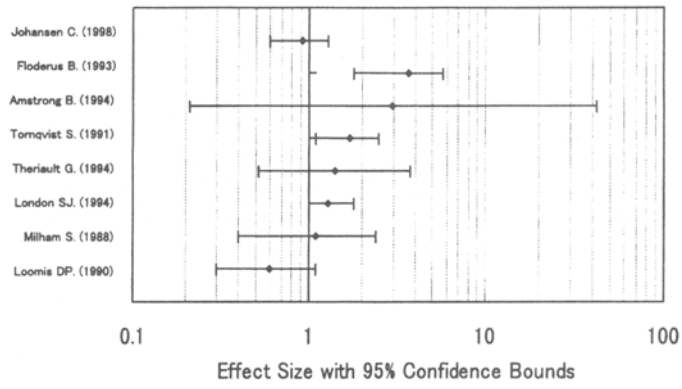

Fig. 4 Epidemiological studies on occupational EMF exposure and adult chronic lymphocytic leukemia

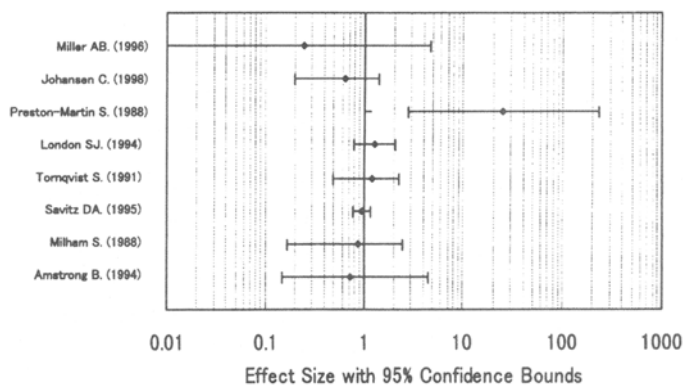

Fig. 5 Epidemiological studies on occupational EMF exposure and adult chronic myeloid leukemia

and Prevention (CDC) in America [7].

Results

Each result of epidemiological studies on occupational electromagnetic field exposure and the risk of adult all leukemia is shown in Fig 1. Of all 22 studies, 10 showed a significant increase in relative risk. In the paper by Richardson et al. [8] 'electrical workers' were studied and the largest risk (relative risk=3.99) of adult all leukemia was shown, but the range of 95% confidence interval was very large, from 1.06 to 14.69. On the other hand, significantly reduced relative risk was reported by Savitz et al. (relative risk: 0.76, 95% confidence interval: 0.64-0.88) [9].

There were only 4 epidemiological studies on the relationship between occupational electromagnetic field exposure and risk of acute lymphocytic leukemia (ALL) (Fig 2). An increased tendency was shown, but because of the small samples of the studies and the wide range of 95% confidence interval of the results, it is difficult to make any conclusion from these results.

Fig 3 shows the results of 12 epidemiological studies of acute myelogenous leukemia (AML). The relative risk of more than 3.0 was reported by Flodin et al. [10], Basuji-Garin et al. [11] and Miller et al. [12]. The results of studies on the relationship between either chronic lymphocytic leukemia (CLL) or chronic myelogenous leukemia (CML) and occupational electromagnetic exposure are

Table 1 **The results of meta-analysis of epidemiological studies on the relationship between occupational electromagnetic fields exposure and the risk of adult leukemia**

Leukemia and subtypes* (references)	RR	95% CI
All Leukemia (22)	1.11	0.98-1.24
ALL (4)	1.38	0.56-2.19
AML (12)	1.07	0.96-1.18
CLL (8)	1.14	0.71-1.57
CML (8)	0.93	0.79-1.08

* ALL: Acute Lymphocytic Leukemia; AML: Acute Myeloid Leukemia; CLL: Chronic Lymphocytic Leukemia; CML: Chronic Myeloid Leukemia

shown in Fig 4 and Fig 5, respectively. The largest relative risk of 3.7 of CLL was suggested by Floderus[13], and 25.4 of CML by Preston-Martin[14]. However, the 95% confidence intervals of the studies were so large that the reliability of the results could not be considered good enough.

The final results of meta-analysis of epidemiological studies on occupational electromagnetic exposure and the risk of adult leukemia are summarized in Table 1. According to the past-published papers that had information on all leukemia, the combined relative risk was only 1.11 (95% confidence interval: 0.98-1.24). The risk increased but not significantly. The combined relative risk of ALL was 1.38, slightly higher than that of all leukemia. However, because of the broad range of 95% confidence interval, the result was not significant. The risks of the other three kinds of leukemia subtypes caused by occupational exposure to an electromagnetic field were not increased significantly either.

Discussion

After the first report by Milham et al.[2] that suggested a higher risk of leukemia incidence among workers exposed to an electromagnetic field occupationally, a number of papers focusing on this issue have been published during the last two decades. Based on these analytical epidemiological studies, the results of our quantitative meta-analysis have not been conclusive on the association between occupational electromagnetic field exposure and the risk of adult leukemia. Exposure assessment of electromagnetic fields was thought to be the most serious deficiency in these published original studies. Occupational title has been utilized almost exclusively as an indirect measure of work exposure. It has raised two key questions: Are workers who hold those job titles truly exposed? And are there other agents present in those work settings that may increase the risk of leukemia? Delpizzo[15] noted that there was substantial misclassification of individual exposures based on using job titles. After entering the 90's, investigators have begun to incorporate magnetic field measurements into the construction of job-exposure matrices as more accurate indicators of electromagnetic field exposure. However, the risks from electromagnetic fields have sometimes weakened according to the results of these studies [16, 17]. Another problem is the assessment of historical exposure to electromagnetic field. Only recently, some studies have documented an individual's time at a particular job during the past several years with an additional measurement of the present exposure level of each job title. Then a job-exposure matrix could be made to get a more accurate assessment of historical exposure to an electromagnetic field in the workplace. A related problem is how to account for duration of exposure from multiple sources. When field measurements have been made in workplaces, values of mean and median are not that much greater than in a residential setting. The types of exposure in the two environments may also be quite different, having varying proportions of long-term, relatively low fields and short-term, intense fields. Multiple exposures from sources other than the workplace should be best assessed through portable measurement.

In the design of future studies, scientists should concentrate on improving the exposure assessment and accounting for various confounders. The occupational studies should include environmental and/or residential exposure, besides the information from the job title or the result of direct or indirect measurement of the electromagnetic field in the workplace. This is most easily accomplished with the use of a portable monitor attached to the subject, in conjunction with an activity diary or an estimate of time spent in different activities. Finally, data on other risk factors should also be gathered, including exposure to carcinogenic chemicals such as benzene and to ionizing radiation (including diagnostic x-ray) at work and at home. Life-style factors like smoking should also be considered.

New occupational studies using job titles alone or primarily are unlikely to add to the present body of knowledge. Answers to the question of electromagnetic fields as a factor to induce cancer will require extensive, carefully designed case-control and cohort studies using the more valid means of exposure assessment.

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