A Japanese study on childhood leukemia in relation to residential background exposure to extremely-low-frequency electromagnetic fields

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Summary

A population-based case–control study was conducted with home interviews in study areas that cover half of Japan. We analyzed 312 case children newly diagnosed during 2.3 years as acute lymphoblastic leukemia (ALL: n=251) or acute myelocytic leukemia (AML: n=61) and their 603 controls (495 for ALL and 108 for AML) matched for gender, age and residential area. An weekly mean MF level in the child's bedroom was used as a measure of exposure. The association was evaluated using conditional logistic regression analysis. For ALL, the odds ratio was 4.73 (95% confidence interval: 1.14-19.7) for the 0.4+ μT category against the reference (< 0.1 μT). The lower MF level categories showed no elevated risk. This dose-response pattern was consistent even when selected confounding factors were included in the models. AML showed no appreciably elevated risk. The elevated risk may be associated with high MF exposures above 0.4 μT for ALL but not for AML. Selection bias alone may not explain the elevated risk.

Introduction

Childhood leukemia has been reported to be associated with residential exposures to power-frequency magnetic fields (MF) since the first study showed an association with a "wire code" in 1979 (Wertheimer *et al*. 1979). Recent two pooled analyses using the data from major studies independently showed an approximately two-fold increase in the risk among children with residential MF exposures above 0.3 or 0.4 μT (Greenland et al 2000, Ahlbom *et a*l 2000). Mainly based on these findings, the IARC review panel concluded that residential MF was a "possible human carcinogen" (IARC 2002). The World Health Organization, however, recommended one or two large epidemiological studies to evaluate the risk with more subjects exposed to high MF (Repacholi *et al* 1999).

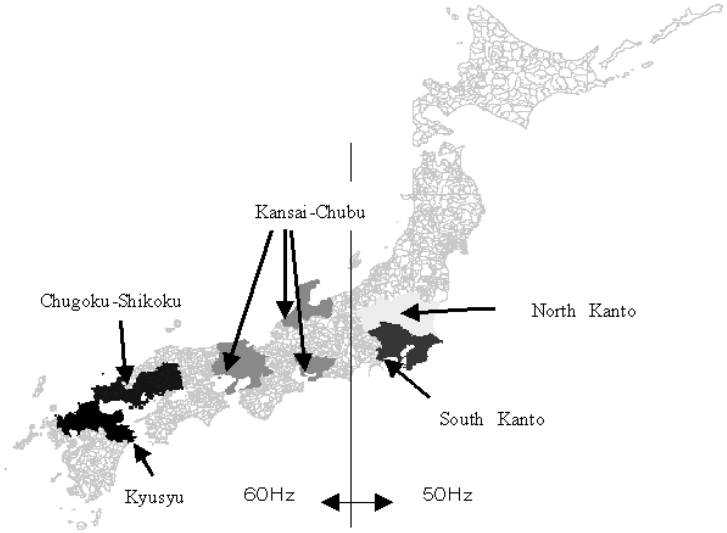
Thus, the present nationwide case-control study was started in 1999 in Japan where high MF exposures were expected.

Materials and Methods

Cases

In this case-control study cases were newly diagnosed children with acute leukemia under age 15 years. The cases were identified during the study period from 1999 to 2001 through 5 childhood leukemia study groups covering virtually all of Japan with 20 million children under age 15 years. Among 1606 patients registered, 791 residing in the study area (Figure 1) covering 53% of the entire Japanese population were asked for participation through attending physicians. 391 (49.4%) agreed and in 312 (79.8%) the study was completed. Excluded from these for analyses were the following: 25 moved; 45 had no EMF measurement; 9 had no control available. The remaining 312 cases were analyzed. The number of patients by type of leukemia was 251 acute lymphoblastic leukemia (ALL) and 61 acute myelogenic leukemia (AML).

Figure1. The study area for the survey.



The study area included 18 prefectures covering 53 % of the total population.

Controls

Controls were selected at random from the list of 123,000 child residents in the study area by matching for age, sex and municipality. 10 matched candidates per case were asked for participation by mail. Case to control ratio aimed at originally was 3 and changed into 2 in the latter half of the study due to the lack of resources. Among the controls who agreed, the top 3 or 2 per case in the original candidate list were selected for analyses. Among 3833 candidates approached, 1097 (28.6%) agreed. Excluded from these for analyses were the following: 60 moved; 403 had no EMF measurement; 31 were excess over the case-control ratio. In the remaining 603 controls (55.0%) the study was completed to be used in analyses. The number of controls by type of leukemia was 495 for ALL cases and 108 for AML cases.

MF measurement

Two types of MF measurements were conducted: one-week-long continuous measurement at 30-second intervals with the EMDEX-Lite (Enertech Co. Ltd; 40Hz-1kHz.) and 5-minute-long spot measurement with the EMDEX-II (Enertech Co. Ltd.; 40- 800 Hz). The child's bedroom was subjected to the former type measurements. The latter type measurements were applied to a room where the child usually spent the longest time daily and up to 4 corners of a detached house, or both entrance and opposite side window of an apartment house. A weekly arithmetic mean MF level in the child's bedroom ("bedroom MF level") was employed as a primary measure of exposure in this study.

Information on possible confounders including the use of electric appliances

Information on the use of electric appliances was collected through home visit by trained interviewers. Asked in the interview were the period and frequency of the use of these appliances. Also asked in the interview were the following: residential history, pesticide exposure of mother during conception and of the child, maternal smoking, drinking and X-ray exposure, immunization on the child, parents' occupation and educational level.

Analyses

Conditional logistic regression analysis was used to estimate odds ratios (OR) and their 95% confidence intervals (CI). The bedroom MF level was categorized into 4 levels with cut-

points of 0.1, 0.2, and 0.4 μT. All the analyses were done by PC-SAS (The SAS software version 8.2, 1999-2001, SAS Institute, Inc., Cary, North Carolina, USA).

Results

The child's bedroom MF level and odds ratios for childhood leukemia (ALL+AML) are shown in Table 1. The odds ratio of the category above 0.4 μT against the reference category below 0.1 μT was 2.63 and it was not statistically significant ($p>0.05$). Controlling for some possible confounding factors did not alter the results appreciably. There was no AML case in the above 0.4+ μT category whereas there were 2 AML controls in that category.

Table 1. Risk of child's bedroom MF level for childhood leukemia (ALL+AML).
Conditional logistic regression analysis

Child's bedroom	Childhood leukemia (ALL+ AML)		
	Cases	Controls	
MF level (μT)	312	603	OR (95%CI)
< 0.1	276	542	1.00
0.1-0.2	18	36	0.94 (0.52 - 1.70)
0.2-0.4	12	20	1.09 (0.52 - 2.32)
above 0.4	6	5	2.63 (0.77 – 8.96)

Table 2 shows the results of the analysis where cases were confined to ALL. The odds ratio in the highest category above 0.4 μT was 4.73 against the reference category below 0.1 μT and it was statistically significant ($p<0.05$). Controlling for some possible confounding factors did not alter the results appreciably. Most of the ALL cases in the highest exposure category had the MF levels far above 0.4 μT. The use of different types of MF measurement such as geometric mean bedroom MF level, nighttime bedroom MF level or daytime bedroom MF level yielded similar results (data not shown).

Table 2. Risk of child's bedroom MF level for ALL alone.
Conditional logistic regression analysis

Child's bedroom	ALL alone		
	Cases	Controls	
MF level (μT)	251	495	OR (95%CI)
< 0.1	223	447	1.00
0.1-0.2	14	29	0.89 (0.46 - 1.75)
0.2-0.4	8	16	1.03 (0.42 - 2.52)
above 0.4	6	3	4.73 (1.14 – 19.7)

Discussion

There are strength and weakness in this study. Some of the strength was the following. The MF measurement was done for a week to counterbalance hourly and daily variations in MF levels. Time difference in the measurement between a case and its controls was short: 2.6 days on the average. A seasonal variation in MF levels was controlled this way. Cases were new cases and the interval between diagnosis and investigation was short: 1.1 years on the

average. This should have reduced loss of memory on confounding factors. Collection of information was done through organized interview by trained interviewers. Thus, differential bias between cases and controls was minimized.

The weakness was a possibility of selection bias resulting from low participation rates both in cases and controls: 49.4% and 28.6% respectively. We examined its possibility in three ways. One was the comparison of the distribution of distance from power lines between participants and non-participants in controls using the address and the geometric information system. The proportion of those residing less than 100m from the nearest high voltage power line was very close: 12.4% among the participants and 11.5% among the non-participants. Another was the examination of reasons for non-participation in cases. Refusal by the families was only 20% among those approached by attending physicians and the majority of the families were not asked for participation by attending physicians for various reasons. The other was analysis based on an assumption which led to the strongest selection bias towards the null. The resultant odds ratio for 4.73 in Table 2 became 1.4 indicating that a selection bias alone could not explain the observed elevated odds ratio in this study. Absence of no elevated risk among AML series also supported small possibility of selection bias.

The proportion of controls with MF exposure above 0.4 μT was quite similar to those in the previous studies (Ahlbom 2000). In this respect Japan was not a country with a high percentage of residents exposed to high MF, as was speculated before this study started. High residential MF levels were attributed not only to high voltage power lines but also to distribution lines of 6.6 kV or 7.7 kV. The MF from these lines and electrical appliances at home may need further attention.

Conclusions

The present study based on weekly measured MF level in child's bedroom showed an increased risk of MF level above 0.4 μT for ALL, but not for the lower MF levels. For AML, no elevated risk was observed. The above results could not be explained by selection bias alone.

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