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Paper

Saito T, Nitta H, Kubo O, Yamamoto S, Yamaguchi N, Akiba S, Honda Y, Hagihara J, Isaka K, Ojima T, Nakamura Y, Mizoue T, Ito S, Eboshida A, Yamazaki S, Sokejima S, Kurokawa Y, Kabuto M. **Power-frequency magnetic fields and childhood brain tumors: a case-control study in Japan**. *J Epidemiol* 2010; 20(1):54-61.

Executive summary

In a population-based case-control study, exposure to power-frequency magnetic fields (MF) of 55 newly diagnosed childhood brain tumor cases was compared with 99 randomly selected sex-, age-, and residential area-matched controls. Compared to the lowest exposure category (<0.1 μT) an odds ratio (OR) of 1.58 (95%-CI: 0.25-9.83) was observed for the exposure category from 0.2 to 0.4 μT based on two exposed cases and four exposed controls. For the highest exposure category (≥0.4 μT) (based on three exposed cases and one exposed control) the OR was estimated to be 10.9 (95%-CI: 1.05-113).

The sample size of this study is very small making the results unstable. Compared to previous studies on this topic, the risk observed is quite likely an overestimation of the true risk, if there is a risk at all. This study should be only considered in the context of a meta-analysis as acknowledged by the authors themselves.

Description of study

Saito et al. conducted a case-control study of brain cancer in children less than 15 years of age and diagnosed between 1999 and 2002 in five geographical regions covering 53.5% (10.7 million) of the total children in Japan. All diagnoses were confirmed histopathologically by one of the authors.

Among the strengths of the study is it's location: the vast majority of previous studies of childhood cancers where in Europe or the USA. The study was initiated in Japan because it was thought that the prevalence of high exposures would be high in this population. The initial expectation that this population would have a large number of highly exposed did not materialize, although exposures were lower than those in the USA and similar to those reported in Europe.

Case and control selection

Cases were selected among 324 in-patients of 107 Japanese hospitals, newly diagnosed with a brain tumor between May 1999 and September 2002, 167 of whom satisfied the eligibility criteria in terms of region of residence.

For each case, up to 3 controls were selected from the resident registration system matched on gender, age and residential area. For each subject, the mother (or if not available a guardian) was interviewed by a trained professional. A modified version of the National Cancer Institute questionnaire was used that requested information about demographic profiles, the medical history of family members, history of changes of residence, type of residence, mother's education, child's history of vaccinations, mother's and child's history of using electric appliances, mother's history of X-ray examinations during pregnancy, mother's medication use, smoking, and alcohol drinking, use of pesticides and other chemicals, and mother's and father's occupational history.

Magnetic field measurement

Residential power in Japan is supplied at 100 volts at a frequency of 50 Hz in Eastern regions (e.g. Tokyo, Yokahama) and 60 Hz in Western regions (e.g. Nagoya, Osaka, Kyoto). Measurements were made in the house the child lived at the time of the survey. The average time between diagnosis and the interview/measurements was 1.1 years. To reduce possible bias due to seasonal variation of MF levels, MF measurements for each set of cases and controls were made close in time and within 12.4 days on average. Based on the family's residential history the length of stay at the current house for the period from birth to the date of diagnosis was assessed.

Exposure assessment included 5-min MF measurements in a room where a child spends the longest time daily, as well as in four corners of the house and at an entrance, and 1-week measurements made in the child's bedroom. Measurements were made away from electrical appliances, with an EMDEX Lite meter. The main exposure metric consisted of a weekly arithmetic mean of the MFs in the child's bedroom, categorized with cut-off points of 0.1, 0.2, and 0.4 μT for comparability with previous studies. The distance from each house to the closest overhead power transmission line (22 kV- 500 kV) located within 100 meters was measured. All conditional logistic regression analyses were adjusted for mother's education as an indicator of socio-economic status.

Results

Using conditional logistic regression analysis and controlling for maternal education the authors estimated the odds ratios (OR) of developing a brain tumor by increasing levels of exposure to extremely low frequency (ELF) magnetic field (0.1-0.2; 0.2-0.4; ≥0.4 vs <0.1 μT). Most children in the study (85% of cases and 87% of controls) were actually unexposed, with 5 cases and 5 controls (9% and 5%) having estimated indoor MF exposure of >0.2 μT. The ORs were 0.74 (95% Confidence Interval (CI) 0.2-3.2) for children classified in the 0.1-0.2 μT category of exposure (based on 3 cases vs 8 controls), 1.58 (95% CI 0.3-9.8) for those in the 0.2-0.4 μT category (2 cases and 4 controls), and 10.9 (95% CI 1.1-113) for the highest exposure level of ≥0.4 μT (3 cases vs 1 control).

All children with MF levels above 0.3 μT (5 cases and 1 control), lived in apartment buildings (distant less than 100 m from a high voltage power line for 3 out of 5 cases). Due to small numbers of cases and controls, the risk estimates observed in the higher categories of exposure are very imprecise (even though statistically significant in the highest category).

Analysis of results

Case/Control selection

In the catchment area there were 167 brain tumour cases during the study period of which 72 (43%) were asked to participate in the study. Some of them (9) did not fulfill eligibility criteria and others were not included for various reasons leaving 55 cases for the analyses (33%). From 692 controls matched to the cases of the catchment area only 99 (14%) were finally considered for the study. Most (503) did not response to the request to participate.

Cases and controls included in the analyses differed by certain characteristics, such as gender (53% of cases were males vs 62% of controls), mothers' education (college/university = 51% of cases' mothers vs 70% of controls' mothers, $p<0.05$), residence type (single family house = 53% of cases vs 67% of controls), and residential mobility (≥80% at time from birth to diagnosis/reference-date spent in current home = 51% of cases vs 58% of controls.

However, cases and controls were comparable in other respects (i.e. length of stay at current house before diagnosis/reference-date ≥12 months = 93% of cases vs 89% of controls; mothers smoking during pregnancy = 11% of both cases and controls; birth order, child's use of electric appliancies and child's immunization).

The authors considered it unlikely that selection bias occurred in the control group, as in a concurrent study of childhood leukemia (Kabuto et al. 2006) the proportion living within 100 m of high voltage power lines was comparable in participant and non participant controls (12% vs 11%, respectively), and the roster of controls was the same as that used in the childhood brain tumor study

Low paticipation rates were observed among both cases and controls, and so participation bias cannot be ruled out if participation was, directly or indirectly, associated to both exposure and disease.

Further, since the percentage of children belonging to well-off families was higher among controls than cases (based on the observed higher prevalences of mothers with college/university education level and of children living in single-family houses vs apartment buildings among controls compared to cases), there is still the possibility of residual confounding by social status.

Measurement of magnetic field exposure

One of the strengths of the study is the exposure assessment. MF exposure of all study participants was measured over one week in the children's bedroom. Additional measurements were conducted in the rest of the apartment/home. Only a few previous studies on this topic have conducted such long-term measurements. Seasonal influence on the measurements was minimized by measuring in apartments/homes of cases and matched controls in close temporal proximity. On average, measurements [in cases] have been conducted 1.1 years after the diagnosis. This is a relatively short interval compared to other studies. Nevertheless, measurements may not exactly represent the MF conditions prior to diagnosis, as the exposure situation may have changed since diagnosis. However, residential history was taken into account and study participants who had moved after the diagnosis were not considered in the analyses. In addition, this kind of uncertainty in exposure classification is most likely randomly distributed among cases and controls and thus would likely result in an underestimation of the true risk than producing a false positive result.

Discussion and conclusions

Due to very small number of cases and controls, especially in the high exposure category, and other drawbacks mentioned above, is very unlikely this study could have any significant impact on the overall scientific evidence concerning possible carcinogenicity of ELF magnetic fields and the related policy implications, as recently assessed by the World Health Organization (2007).

Some 16 epidemiologic studies examining the potential association between residential exposure to MFs and childhood brain tumors have been published. Individual studies of brain cancer, usually suffering from even smaller numbers of exposed cases than the leukaemia studies, have generally been unable to examine the potential association with high MF exposure with satisfactory statistical precision. In a recent meta-analysis the observed summary shows estimates were close to one with relatively narrow 95% confidence intervals including one in all analyses. Thus this meta-analysis overall found no increase in childhood brain cancer risk, with the exception of high cut-point analyses (0.3/0.4 μT), where the possibility of a moderate risk increase could not be excluded (Mezei et.al. 2008).

References

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