

Exposure to electromagnetic fields and cancer: the epidemiological evidence

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Abstract

There is still an ongoing scientific controversy whether exposure to electromagnetic fields is associated with an increased cancer risk in humans. Epidemiological studies have shown a consistent association between exposure to extremely low-frequency (ELF) magnetic fields and the risk of leukemia in children, but even after decades of investigations it is unclear whether the observed association is causal or due to bias and limitations of the studies. The International Agency for Research on Cancer (IARC) has therefore classified ELF magnetic fields as possibly carcinogenic to humans. Several studies of different designs investigated the association between radiofrequency (RF) electromagnetic fields related to the use of cellular telephones and the risk of brain tumors. While short-term use of cell phones of less than ten years was not related to any increased tumor risk, uncertainty remains particularly for longer term heavy users. Cell phone studies are methodologically challenging and future study protocols need to reduce limitations observed in studies available today.

1. Introduction

Exposure to electric, magnetic and electromagnetic fields in low and high frequency ranges is ubiquitous in modern society. Consequently, even small health risks could have large effects on a population level, as exposures are so widespread. Regarding extremely low-frequency (ELF) magnetic fields there is little evidence for any increased cancer risk, except the observation of an increased risk of childhood leukemia at rare exposure levels of 0.3-0.4 μT or higher. Based on these observations, in 2002, the International Agency for Research on Cancer has classified ELF magnetic fields as a possible carcinogen. In recent years research has focused on radiofrequency (RF) electromagnetic fields emitted from cellular telephones and, as the devices are held directly to the head, specifically investigated the risk of different types of brain tumors. The classification of RF was performed in May 2011.

2. ELF magnetic fields and the risk of leukemia in children

Childhood cancer under the age of 15 years is rare accounting for less than 1% of all neoplasms diagnosed each year in developed countries. Acute leukemias are the most common malignancy in children, accounting for a third of all diagnoses. The incidence rate of acute leukemias ranges from 30-50 per 1 million children per year. The most recent data on incidence trends indicate a small annual increase of 0.7% in European countries in the last three decades [1], however, some of the increase is likely to be attributable to progresses in childhood cancer classification and registration. The biological heterogeneity of childhood leukemia is well documented and it is therefore unlikely that there is a single causal exposure or mechanism [2]. Little is known about the etiology of childhood leukemia; only few genetic predispositions and high doses of ionizing radiation have been established as risk factors.

ELF magnetic fields have been studied as a risk factor for childhood leukemia since the late 1970s. At present, more than 20 epidemiological studies have investigated this topic, with significant improvements in study designs and methods of exposure assessment over time. These studies have been pooled in separate meta-analyses. Greenland et al. pooled all available studies, however, they had to combine various exposure indices into one single metric. They reported a combined relative risk estimate for leukemia of 1.7 (95% confidence interval (CI) 1.2-2.3) in children exposed to average magnetic fields above 0.3 μT compared to those exposed below 0.1 μT [3]. Ahlbom et al. only pooled studies that fulfilled certain inclusion criteria such as a defined population base for case ascertainment and control recruitment and usage of long term measurements or historical magnetic field calculations for exposure assessment. They reported a relative risk estimate of 2.0 (95% CI 1.3-3.1) for exposures $\geq 0.4\mu\text{T}$ compared to exposures below 0.1 μT [4]. A shortcoming was that the possibilities for dose-response analyses were limited, as only very few children were exposed to average magnetic fields of 0.4 to 1 μT or higher. Hence, data were too sparse to reliably predict the shape of a dose-response curve for magnetic fields higher than 0.4 μT and this shape is more or less

compatible with trends ranging from a further increase in risk, to a constant risk or even a downward gradient. Even in the intermediate exposure range between 0.1 and 0.4 μT there is some statistical uncertainty and, hence, it is not clear what the best dose-response model would be. While the meta-analysis of Ahlbom et al. rather suggests a risk increase at 0.4 μT but not below, an extension of this analysis by Schüz et al. looking specifically at night-time exposures finds a log-linear model as a suitable approximation of a trend [5]. More recently, studies published after these first meta-analyses were gathered and pooled by Kheifets et al., confirming the association shown in the previous pooling projects [6]. Overall, evidence from animal studies or in vitro studies neither support nor contradict the epidemiological findings. Recent studies on ELF magnetic fields and survival after childhood leukemia show a somewhat poorer survival with increasing exposure, but based on very small numbers and follow up of this hypothesis is required [7, 8]. It may suggest, however, that ELF magnetic fields promote the growth of leukemia cells resulting in a relapse.

It cannot be excluded that the observed association, although emerging in different studies, is due to methodological limitations. Particularly in studies measuring magnetic fields participation rates were low, thus, the study populations might have been not representative to investigate the association. Simulation studies using the dataset of the German study suggest that 66% of the observed association were attributable to bias and error [9]. This suggests an overestimation of the strength of the association, but raises the question whether bias explains the association in its entirety [10].

3. Cellular telephone use and the risk of brain tumors

Glioma and meningioma are the most common types of brain tumors in adults. Glioma, comprising mainly highly malignant tumors with poor prognosis, occur more often in men, with incidence rates between 2-4 per 100,000 men in 20-39 year olds, 8-10 per 100,000 in 40-59 year olds, and around 15 per 100,000 in 60-79 year olds; respective incidence rates in women are 2-3, around 5 and around 10 in the according age groups. Meningioma, a benign brain tumor, occurs more often in women, with incidence rates of 1-2/100,000, 4-8/100,000 and 10-15/100,000 in the 20-39, 40-59 and 60-79 year olds, whereas respective rates in men are low with <1, 2-3 and around per 100,000. Overall, incidence rates of brain tumors have been rising over the last decades, mainly attributable to a 50% increase of meningioma in women above age 50 years. Glioma incidence rates in young and middle-aged men, on the other hand, which would be the relevant age- and sex-specific subgroup in which a cell phone-related effect should be observed the earliest, were stable or even slightly decreasing, providing some evidence against a substantial risk associated with cell phone use that might have occurred before 2003 [11].

Further evidence against an association comes from a Danish nationwide cohort study, following 420,000 cell phone subscribers for occurrence of cancer up to 2002 [12]. Case-control studies on the topic have not been consistent, with a study from Sweden showing increased relative risks that appear to be incompatible with the observation of no increase in the time trends of incidence rates [13]. The largest case-control study, the Interphone study coordinated by the International Agency for Research on Cancer, did not show an overall increased risk, but a somewhat elevated risk estimate in the group of heaviest cumulative use [14]. This effect might be causal or due to limitations of the study, as methodological studies yielded substantial reporting error when participants were asked about their cell phone use back in time.

4. Conclusions

Electromagnetic fields remain an exposure of high public concern, although the scientific evidence suggests, in respect to cancer, rather no or at most moderate effects. Cellular telephones, however, are still a relatively recent technology, thus, given usually long induction periods of cancer further research is warranted to investigate whether there is a long-term effect that was not detectable until now. Shorter term use, i.e. not longer than 10-15 years, does not appear to be related to any substantial brain tumor risk, as time trends in incidence rates have been stable, cohort studies showed no associations, and case-control studies showed at most modest risk increases in sub-groups that might well be attributable to methodological limitations. Prospective cohort studies are recommended to be the way forward and a joint European approach has recently started [15]. Whether the association between ELF magnetic fields and childhood leukemia is causal remains a scientific controversy; although the epidemiological evidence is consistent, no plausible mechanism to explain the observed association has been proposed so far. If the association is causal, it is estimated that about 1% of all childhood leukemia would be attributable to ELF magnetic fields in Western European countries while this proportion would be 2-3% in North America, with little data for profound estimations in other parts of the world

[16]. It is unlikely that further epidemiological studies will enhance the field and the focus should be on experimental and mechanistic studies.

It is at present unclear when science can provide more reliable evidence, given that the ELF magnetic fields debate awaits its breakthrough since several decades. The situation is somewhat different for cellular telephones, as due to the widespread use, risks will ultimately impact incidence rates of diseases. Policy makers and individuals may consider precautionary options, such as using wired hands-free devices when using cell phones, restricting cell phone use in children and considering exposure reduction measures when planning the building of new power lines.

5. References

1. Steliarova-Foucher E, Stiller C, Kaatsch P, Berrino F, Coebergh JW, Lacour B, et al. Geographical patterns and time trends of cancer incidence and survival among children and adolescents in Europe since the 1970s (the ACCISproject): an epidemiological study. *Lancet* 2004; 364:2097-105.
2. Biondi A, Cimino G, Pieters R, Pui CH. Biological and therapeutic aspects of infant leukemia. *Blood* 2000; 96:24-33.
3. Greenland S, Sheppard AR, Kaune WT, Poole C, Kelsh MA. A pooled analysis of magnetic fields, wire codes, and childhood leukemia. Childhood Leukemia-EMF Study Group. *Epidemiology* 2000; 11:624-34.
4. Ahlbom A, Day N, Feychting M, Roman E, Skinner J, Dockerty J, et al. A pooled analysis of magnetic fields and childhood leukaemia. *Br J Cancer* 2000; 83:692-8.
5. Schüz J, Svendsen AL, Linet M, McBride ML, Roman E, Feychting M, et al. Night-time exposure to electromagnetic fields and childhood leukemia: an extended pooled analysis. *Am J Epidemiol* 2007; 166:263-9.
6. Kheifets L, Ahlbom A, Crespi CM, Draper G, Hagihara J, Lowenthal RM, et al. Pooled analysis of recent studies on magnetic fields and childhood leukaemia. *Br J Cancer* 2010; 103:1128-35.
7. Foliart DE, Pollock BH, Mezei G, Iriye R, Silva JM, Ebi KL, et al. Magnetic field exposure and long-term survival among children with leukaemia. *Br J Cancer* 2006; 94:161-4.
8. Svendsen AL, Weihkopf T, Kaatsch P, Schüz J. Exposure to magnetic fields and survival after diagnosis of childhood leukaemia - a German cohort study. *Cancer Epidemiol Biomarkers Prev* 2007; 16:1167-71.
9. Schüz J. Implications from epidemiologic studies on magnetic fields and the risk of childhood leukemia on protection guidelines. *Health Phys* 2007; 92:642-8.
10. Schüz J, Ahlbom A. Exposure to electromagnetic fields and the risk of childhood leukaemia: a review. *Radiat Prot Dosimetry* 2008; 132:202-11.
11. Deltour I, Johansen C, Auvinen A, Feychting M, Klæboe L, Schüz J. Time trends in brain tumor incidence rates in Denmark, Finland, Norway and Sweden, 1974-2003. *J Natl Cancer Inst* 2009; 101:1721-4.
12. Schüz J, Jacobsen R, Olsen JH, Boice JD Jr, McLaughlin JK, Johansen C. Cellular telephone use and cancer risk: an update of a nationwide Danish cohort. *J Natl Cancer Inst* 2006; 98: 1707-13
13. Hardell L, Mild KH, Carlberg M, Söderqvist F. Tumour risk associated with use of cellular telephones or cordless desktop telephones. *World J Surg Oncol* 2006; 4:74.
14. The Interphone Study Group. Brain tumour risk in relation to mobile telephone use: results of the INTERPHONE international case-control study. *Int J Epidemiol* 2010; 39: 675-94.
15. Schüz J, Elliott P, Auvinen A, Kromhout H, Poulsen AH, Johansen C, et al. An international prospective cohort study of mobile phone users and health (Cosmos): Design considerations and enrolment. *Cancer Epidemiol* 2011; 35:37-43

16. Maslanyj M, Lightfoot T, Schüz J, Sienkiewicz Z, McKinlay A. A precautionary public health protection strategy for the possible risk of childhood leukaemia from exposure to power frequency magnetic fields. *BMC Public Health* 2010; 10:673.