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Brief Communication

Magnetic Field Exposure and Prognostic Factors in Childhood Leukemia

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We examined the association between magnetic field (MF) exposure and the presence of prognostic risk factors among 482 children diagnosed with acute lymphoblastic leukemia (ALL) between 1996 and 2001. Personal 24-h MF measurements were obtained for 412 children; 386 children were included in analyses. There were no trends seen between increasing exposure to MF and the presence of adverse clinical and tumor-specific prognostic factors. Our results suggest that exposure to MF is not associated with the presence of unfavorable cytogenetic abnormalities in leukemic blast cells or with clinical factors at the time of diagnosis that predict poor survival. Bioelectromagnetics 28:69–71, 2007.

Key words: electromagnetic fields; leukemia; lymphoblastic leukemia

Over the last three decades, childhood acute lymphoblastic leukemia (ALL) has been transformed from a disease with a less than 30% 5-year survival rate to one in which over 80% of affected children will survive [Pui and Evans, 2006]. Two important clinical factors that predict poor survival are the age of the child at diagnosis (with infants and older children at higher risk) and high white blood cell count at diagnosis. The presence of a mediastinal mass and central nervous system involvement at diagnosis are also markers of tumor burden and are associated with poor prognosis. Tumor-specific factors identified during cytogenic analysis of the leukemia blast cells, such as an alteration in chromosomal number, trisomies, and translocations, have an impact on survival [Armstrong and Look, 2005]. Low DNA Index is an unfavorable marker, as blast cells displaying chromosomal loss are less responsive to chemotherapy than are hyperdiploid cells. The presence of certain translocations portends a poor outcome, while the presence of trisomies 4 and 10 is favorable [Sutcliffe et al., 2005]. Gender, ethnic, and racial survival differences have decreased as overall survival has improved [Pui et al., 2004].

While epidemiologic studies have focused on environmental exposure to magnetic fields (MF) and leukemia incidence, studies have not evaluated the possible direct or indirect role of MF exposure on disease relapse and survival. Our study addressed two questions: (1) does exposure to MF influence particular chromosomal rearrangements or other leukemia characteristics detected at the time of

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diagnosis that predict relapse and poor survival; and (2) is exposure to MF an independent factor in long-term survival? Results of the survival analysis have been published, and while we report poorer survival among children in the highest MF exposure category, the small numbers limited inferences for this finding [Foliart et al., 2006]. We now report the relationship between MF exposure and leukemia prognostic factors assessed at diagnosis.

During the accrual period of September 1996 to January 2001, 482 children at the 51 participating Pediatric Oncology Group (POG) centers enrolled onto

TABLE 1. Association Between Prognostic Factors and Magnetic Field Exposure[a]

	<0.1 μT		0.1–1.9 μT		0.2–0.29 μT		≥0.3 μT		
Factor at diagnosis[b]	#	%	#	%	#	%	#	%	Total
Age									
<6 years	181	66	63	23	17	6	13	5	274
≥6 years	70	63	32	29	4	4	6	5	112
White blood cell count									
<50,000 cells/mm^3	215	67	77	24	16	5	15	5	323
≥50,000 cells/mm^3	36	57	18	29	5	8	4	6	63
Immunophenotype									
B-precursor	235	65	89	25	19	5	18	5	361
T-cell	16	70	4	17	2	9	1	4	23
B-cell	0	0	2	100	0	0	0	0	2
Gender									
Female	114	61	50	27	14	8	18	4	186
Male	137	69	45	23	7	4	11	6	200
NCI risk group									
Low risk	173	66	60	23	15	6	14	5	262
High risk	78	63	35	28	6	5	5	4	124
Race/ethnicity									
White	194	67	69	24	15	5	12	4	290
Nonwhite	57	59	26	27	6	6	7	7	96
Initial platelet count									
<100,000 platelets/mm^3	161	64	64	26	12	5	14	6	251
≥100,000 platelets/mm^3	69	68	22	22	7	7	3	3	101
Mediastinal mass									
Absent	220	65	83	25	18	5	17	5	338
Present	11	73	3	20	1	7	0	0	15
DNA index (DI)									
Low risk (>1.16)	69	62	28	25	3	3	11	10	111
High risk (≤1.16)	180	66	66	24	18	7	8	3	272
Translocation t(9;22)									
Absent	202	66	76	25	16	5	14	5	308
Present	1	33	2	67	0	0	0	0	3
Translocation t(4;11)									
Absent	204	66	77	25	16	5	14	5	311
Present	3	75	1	25	0	0	0	0	4
Translocation t(1;19)									
Absent	199	65	77	25	15	5	14	5	305
Present	8	80	1	10	1	10	0	0	10
Trisomy 21									
Present	80	63	32	25	6	5	8	6	126
Absent	105	68	38	25	8	5	4	3	155
Trisomy 8									
Present	27	61	12	27	1	2	4	9	44
Absent	158	67	58	24	13	5	8	3	237
Trisomies 4 and 10									
Present	45	60	20	27	2	3	8	11	75[c]
Absent	155	67	57	25	13	6	6	3	231

[a]Exposure classified by 24 h time weighted average (TWA).
[b]For each prognostic factor, the low risk category is presented on the first row, high risk on second row.
[c]$P = 0.05$, two-sided Cochran–Armitage trend test.

the study. The study protocol was approved by the institutional review boards of the Public Health Institute and each participating treatment center, and was in accord with all relevant laws and regulations. Written informed consent was obtained from all participants and/or their parents/legal guardians.

The age of study subjects ranged from 1 to 15 years. Twenty-nine per cent (482/1672) of all eligible children who were being treated on POG therapeutic protocols enrolled onto this study. Details of the methods have been published [Foliart et al., 2001, 2002, 2006].

At the time of diagnosis, all children had blood and bone marrow samples sent to a central laboratory at the University of Alabama, Birmingham, for cytogenetic analysis. Personal, 24 h MF exposure assessment was initiated after the child completed induction therapy and was undergoing consolidation therapy as an outpatient. Exposure was monitored using the EMDEX Lite meter (Enertech Consultants, Campbell CA, USA). The meter, teddy bear backpack or waist pack, and written with pictoral instructions (in English, Spanish, or French), were forwarded to families and returned by mail.

Of the 482 enrolled children, 412 (85%) completed the first-year MF assessment protocol and 386 (80%) were eligible for inclusion in analysis. Four mutually exclusive categories of TWA ($<0.1, 0.1–0.19$, $0.2–0.29$, >0.3 μT) and the following cytogenetic factors were examined: DNA Index, translocation t(9;22), translocation t(4;11), translocation t(1;19), trisomy 21, trisomy 8, and trisomies 4 and 10. Analyses were also conducted for clinical prognostic factors that predict poor prognosis: age at diagnosis older than 6 years, male gender, nonwhite race/ethnicity, initial white blood cell greater than 50 000 cells/mm^3, initial platelet count greater than 100 000 cells/mm^3, and presence of a mediastinal mass. Each of these dependent variables was compared with TWA as the independent variable. The Cochran–Armitage test was used for trend analysis.

Of the 386 children included in analysis, 71% were younger than 6 years old, with 29% aged 6–15 years. Boys slightly outnumbered girls 52–48%. The mean 24-h TWA was 0.11 μT (mean 24-h GM = 0.075 μT), with a 95th percentile value for our cohort of 0.3 μT.

Table 1 details the distribution of prognostic factors by MF exposure, with TWA as the metric (results using GM were similar and are not presented). There were no trends seen between increasing exposure to MF and the presence of factors at diagnosis that predict a poor prognosis. Children with exposures ≥ 0.3 μT were more likely to have trisomies 4 and 10 in leukemia blast cells, a favorable prognostic factor (two-sided exact test of trend, $P = 0.05$). The clinical inferences of this finding are limited and may be attributable to chance alone. There were no associations between race and prognostic factors (data not presented).

We had hypothesized that MF exposure preceding the diagnosis of ALL may influence the occurrence of tumor-specific prognostic factors, thereby exerting an indirect effect on survival. However, we found no associations between MF exposure and unfavorable tumor or clinical factors based on MF exposures monitored shortly after diagnosis. Our results suggest that exposure to MF is not associated with recurrent cytogenetic abnormalities in leukemic blast cells or with poor prognostic features at the time of diagnosis of ALL.

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