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Mobile phones, cordless phones and brain tumour risk in different age groups

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Introduction

The use of wireless phones has increased rapidly world wide since the late 1990's, and the prevalence has reached one hundred percent in many countries. Cell phone technology incorporates base stations, transmission tower antennae, and cell phone hand-held units. Concerns over various risks have been raised, particularly an increased risk for brain tumours (Hardell, Sage 2008). The ipsilateral brain (same side as the mobile phone has been used) is most exposed, whereas the contralateral side (opposite side to the mobile phone) is much less exposed (Cardis et al 2008). Thus it is of vital importance to have information for risk assessment on the localisation of the tumour in the brain and which side of the head that has predominantly been used during phone calls.

Sweden was one of the first countries in the world to adopt this new technology, so studies on health effects from the wireless technology may be especially pertinent in our country for early warnings on health risks. Analogue phones (NMT; Nordic Mobile Telephone System) were introduced on the market in the early 1980´s using both 450 and 900 Megahertz (MHz) fields. NMT 450 was used in Sweden from 1981 to December 31, 2007, whereas NMT 900 operated between 1986 and 2000.

Today the digital system (GSM; Global System for Mobile Communication) is the dominant transmission type. It started in 1991 and uses dual band, 900 and 1,800 MHz. The third generation of mobile phones, 3G or UMTS (Universal Mobile Telecommunication System), using 1,900 MHz radio frequency (RF) fields has been introduced worldwide for just a few years, starting in Sweden in 2003.

Desktop cordless phones called DECT (Digital Enhanced Cordless Telecommunication) were introduced in Sweden in 1988 and are widely used. DECT first used analogue 800-900 MHz RF fields, but transitioned to digital 1900 MHz in the early 1990's.

Since it usually takes decades for cancer development after exposure to a carcinogen it is especially pertinent to study long-term health effects from use of wireless phones in our country. So far our case-control studies on use of wireless phones and risk for brain tumours are among the largest published in the world from a single research unit (Hardell et al 2006a,b). They were all approved by the local ethical committees and followed the same study protocol. A short summary of these studies is given below. Results are also presented from a recent meta-analysis on use of mobile phones and the risk for brain tumours (Hardell et al 2009). This paper presents most recent results of all publications through 2009 from the Hardell group and updates our previous analyses.

Materials and Methods

Our first case-control study on brain tumours and use of mobile phones was published in 1999 (Hardell el al 1999). In total 209 (90 %) of the cases and 425 (91 %) of the controls that fullfilled the inclusion criteria answered the mailed questionnaire. However, this was a rather small study and no firm conclusions could be drawn on an association, although a somewhat increased risk was found for ipsilateral mobile phone use (Hardell et al 1999, 2001). Furthermore, use of cordless phones was not assessed, as was done in our subsequent studies.

The second case-control study included cases diagnosed during the time period January 1, 1997 through June 30, 2000 and population based controls. This study was followed by our third case-control study on the same topic. The methods were the same as in the second study using an identical questionnaire. The study period was from July 1, 2000 until December 31, 2003.

In further analysis we pooled the cases and controls from the second and third studies. The following results are thus based on 905 (90 % responding persons) cases with malignant and 1 254 (88 %) cases with benign brain tumour that answered the questionnaire. One case had both acoustic neuroma and meningioma and another case had both 'other type' of malignant tumour and acoustic neuroma. For comparison 2 162 (89 %) population based controls were used. The results from the pooled analysis have been published previously with references to the separate studies (Hardell et al 2006 a,b). In the following tables in this summary some additional results are presented, especially regarding age at first use of a mobile or cordless phone. In these calculations we included in ipsilateral exposure also equally varying use of both ears (50 % left side and 50 % right side), whereas contralateral exposure was < 50 % of the calling time.

Statistical methods

Unconditional logistic regression analysis was used for calculations of odds ratio (OR) and 95 % confidence interval (CI) using StataSE 10.1 (Stata/SE 10.1 for Windows; StataCorp., College Station TX). Adjustment was made for sex, age (as a continuous variable), socio-economic index (SEI) and year of diagnosis. The same year as for the case was used for the corresponding control. The unexposed category consisted of subjects that reported no use of cellular or cordless phones or only had used a wireless phone the year before tumor diagnosis (corresponding year for the matched control). Note, that laterality of the tumour was not available for all cases, e.g., midline tumours or tumours in both hemispheres. We used fixed effects model for calculation of odds ratio (OR) and 95 % confidence interval (CI) in the meta-analysis of all published studies in this area, as further explored in another publication (Hardell et al 2009).

Results

Different tumour types in the Hardell group studies

For astrocytoma grade I-IV mobile phone use yielded OR = 1.4, 95 % CI = 1.1-1-7 increasing to OR 2.0, 95 % CI = 1.5-2.5 for ipsilateral use, whereas no increased risk was found for contralateral use, Table 1. OR increased further using > 10-year latency period for all use to OR 2.7, 95 % CI = 1.8-3.9 and for ipsilateral use to OR = 3.3, 95 % CI = 2.0-5.4. Also cordless phones yielded significantly increased risk for astrocytoma. For 'other' types of

malignant brain tumours the risk was significantly increased for mobile phone use in the > 10 year latency group, highest in the ipsilateral group with OR = 2.6, 95 % CI = 1.2-5.8.

In Table 2 results are presented for acoustic neuroma. For use of mobile phone OR = 1.7, 95 % CI = 1.2-2.3 was calculated, and for cordless phone OR = 1.5, 95 % CI = 1.04-2.0. Higher ORs were calculated for ipsilateral use, whereas no significantly increased ORs were found for contralateral use. Ipsilateral use in the > 10 year latency period yielded for mobile phone OR = 3.0, 95 % CI = 1.4-6.2, and for cordless phone OR = 2.3, 95 % CI = 0.6-8.8.

Regarding meningioma ipsilateral mobile phone use gave OR = 1.3, 95 % CI = 1.01-1.7 increasing to OR = 1.6, 95 % CI = 0.9-2.9 in the > 10 year latency group, Table 2. For cordless phones highest OR was calculated using > 10 year latency period, OR = 3.0, 95 % CI = 1.3-7.2 in the ipsilateral group. For other types of benign brain tumours no clear pattern of an association was found, although > 10 year latency use of mobile phone yielded OR = 4.7, 95 % CI = 1.1-21 in the ipsilateral group. These results were however based on only 4 exposed cases, Table 2.

Age at first use of wireless phones

Subjects with first use of mobile phone < 20 years of age had highest risk for astrocytoma, OR = 5.2, 95 % CI= 2.2-12, Table 3. Also for cordless phones highest OR was found in that age group, OR = 4.4, 95 % CI = 1.9-10. Lower ORs were calculated for first use of a wireless phone at higher age. Similar results were found for acoustic neuroma; for mobile phone OR = 5.0, 95 % CI = 1.5-16 in the youngest age group, Table 3. Regarding cordless phone only one case had first use < 20 years age, so no conclusions could be drawn. The same calculations for meningioma gave no significantly increased ORs in the different age groups (data not in Table).

Meta-analysis of all published case-control studies

As has been discussed elsewhere most results in early studies on this topic were based on short latency periods (Hardell et al 2009). To evaluate true brain tumour risk, a longer latency period of perhaps decades may be necessary (Sage, Carpenter 2009). Only the Hardell group and some of the Interphone studies have presented risk for latency period of at least 10 years. In contrast to the Hardell group almost all of the Interphone studies included use of cordless phones in the “unexposed” group; in two of these studies only briefly mentioned without proper result presentation (Hardell et al 2008a). A Danish cohort study on persons who were registered for the use of mobile phones sometimes during 1982-1995 was not included due to several methodological shortcomings as discussed in detail elsewhere (Hardell et al 2008a). Thus, for example more than 200 000 corporate subscribers were excluded, i.e. the heaviest users, and no data on laterality of tumour in relation to mobile phone use were presented. Such omission could dilute any observable risks.

Table 4 presents a summary of the results for latency period of 10 years or more, for furhter details see Hardell et al (2009). For glioma a significantly increased risk was found for ipsilateral mobile use, OR = 1.9, 95 % CI = 1.4-2.4, and for acoustic neuroma OR = 1.6, 95 % CI = 1.1-2.4. However, the risk was not significantly increased for meningioma.

Discussion

A consistent pattern of an association between use of mobile or cordless phones and ipsilateral astrocytoma and acoustic neuroma was found in the studies from the Hardell group. The risk increased for both tumour types with time since first use and was highest in the group with > 10 year latency. For biological reasons this is what one would expect for a carcinogenic effect for use of wireless phones. The brain is a near-field organ for such exposure and highest risk in the > 10 year latency period would be expected. Aspects on the used methods, interpretation of results and discussion of other studies in this area may be found in our different studies in this area as has previously been published (Hardell et al 2008a,b, 2009).

No other studies than from the Hardell group have published comprehensive results for use of cordless phones. As we have discussed in our publications it is pertinent to include also such use in this type of studies. Cordless phones are an important source of exposure to microwaves and they are usually used for a longer time period on daily basis as compared to mobile phones. Thus, to exclude such use, as was done in e.g. the Interphone studies, could lead to an underestimation of the risk for brain tumours from use of wireless phones.

Of special concern is the five-times higher risk for both astrocytoma and acoustic neuroma among cases that started mobile phone use before the age of 20. Similar results were found for astrocytoma and cordless phone use. The results were based on low numbers of exposed cases and controls, but are still statistically significant. Regarding acoustic neuroma and cordless phones the results were inconclusive, since only one case had used a cordless phone before the age of 20. A much lower risk was found in older age groups. From a biological point of view these results are credible since the developing brain would be more sensitive to carcinogens. These results are worrying regarding children since the brain is more exposed to microwaves during mobile phone calls in young persons due to smaller head and thinner bone, as has been discussed elsewhere (Cardis et al 2008, Sage, Carpenter 2009).

The meta-analysis on use of mobile phones and the association with brain tumours included all case-control studies that we have identified in the peer-review literature. Most studies have published data with rather short latency period and limited information on long-term users, and the results using 10 year latency period are based on rather low numbers. In spite of that, also the meta-analysis yielded a consistent pattern of an increased risk for acoustic neuroma and glioma after > 10 years mobile phone use, thus supporting the results from the Hardell group.

Finally it should be mentioned that overall results on this topic from the Interphone study group yet have not been published. These studies were performed in 13 countries and used a common protocol. The study center is International Agency for Research on Cancer (IARC) in Lyon, France, and a substantial amount of the grants comes from the telecom industry. Also, according to the contract, the industry has full access to the results one week before publication. So far, only results from eight of the participating countries have been published and were all included in the above presented meta-analysis. The period for inclusion of cases was 1999-2004, somewhat varying for different countries, and it is unclear why the final results have not been published, now five years later. Certainly the Interphone study group has a high responsibility to publish its overall results promptly, not the least from a public health perspective, and not to delay the results further.

It should be pointed out that in the Swedish part of the Interphone studies, one of the authors (Ahlbom) had stated in an 'opinion' letter, even before the study started, that an asserted association between cellular telephones and brain tumours is 'biologically bizarre' (Adami et al 2001). This statement might preclude him from objectivity in his own investigation and has been rebutted (Hardell et al 2007). The so called REFLEX-study indicates that there are in fact biological mechanisms that could link exposure to the development of diseases such as brain tumours (REFLEX 2005).

Interestingly, one of the authors of the 'opinion' letter, Professor Adami together with Professor Trichopoulus stated in an Editorial (Trichopoulus, Adami 2001) in the same issue of New England Journal of Medicine as the US study on mobile phone use and brain tumours by Inskip et al (2001) was published that …'the use of cellular telephones does not detectably increase the risk of brain tumours' and that 'This study allays fears raised by alarmist reports that the use of cellular telephones causes cancer'. This statement goes far beyond what is scientifically defensible, e.g. longest duration for use was only $\geq$ 5 years and no data with 10 years latency were presented. Maybe this editorial was biased by not reported conflicts of interest (Hardell el 2007, Michaels 2008).

Also another person who participated in the Swedish part of the Interphone studies, Feychting, has made a most remarkable comment on our studies when she "wonders if the questions really were placed in the same way to cases and controls" (Björkstén 2006). For methodological reasons this comment is of course not true and casts doubt on her scientific credibility and the quality of her own research methods. Certainly these circumstances show how economical and other not disclosed interests may influence this research area and preclude objective risk evaluation. Still these attacks on our research are few in an international perspective and almost exclusively made by a few Swedish researchers with their own not disclosed research agenda (Hardell et al 2007). This type of unfounded critique needs to be rebutted and is quite in contrast to some recent international publications (Kundi 2009, Mead 2009).

In summary there is consistent evidence of an increased risk for glioma and acoustic neuroma after > 10 years latency for use of mobile or cordless phones. Especially worrying is the finding of highest risk in persons with first use of a mobile phone before the age of 20 in the study from the Hardell group. The current guideline for exposure to microwaves from wireless phones is not safe and needs to be revised.

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Table 1. Odds ratio (OR) and 95 % confidence interval (CI) for malignant brain tumours. Numbers of exposed cases (Ca) and controls (Co) are given. Adjustment was made for age, sex, SEI, and year of diagnosis.

Type of tumour/ Type of telephone	All Ca/Co OR (CI)	Ipsilateral + Ipsi/contralateral Ca/Co OR (CI)	Contralateral Ca/Co OR (CI)
Astrocytoma, grade I-IV (n=663)			
Mobile phone, > 1 year latency	346/900 1.4 1.1-1.7	229/374 2.0 1.5-2.5	98/308 1.0 0.7-1.4
>10 year latency	78/99 2.7 1.8-3.9	50/45 3.3 2.0-5.4	26/29 2.8 1.5-5.1
Cordless phone, > 1 year latency	261/701 1.4 1.1-1.8	167/309 1.8 1.4-2.4	81/235 1.2 0.8-1.6
>10 year latency	28/45 2.5 1.4-4.4	19/15 5.0 2.3-11	8/20 1.4 0.6-3.5
Other malignant (n=242)			
Mobile phone, > 1 year latency	122/900 1.2 0.9-1.7	65/374 1.4 0.9-2.1	39/308 1.0 0.6-1.5
>10 year latency	18/99 2.2 1.1-4.1	11/45 2.6 1.2-5.8	4/29 1.6 0.5-5.2
Cordless phone, > 1 year latency	89/701 1.2 0.8-1.7	40/309 1.0 0.6-1.6	35/235 1.2 0.7-1.8
>10 year latency	5/45 1.3 0.4-3.7	1/15 0.7 0.1-5.9	4/20 2.3 0.7-7.8

Table 2. Odds ratio (OR) and 95 % confidence interval (CI) for benign brain tumours. Numbers of exposed cases (Ca) and controls (Co) are given. Adjustment was made for age, sex, SEI, and year of diagnosis.

Type of tumour/ Type of telephone	All Ca/Co OR (CI)	Ipsilateral + Ipsi/contralateral Ca/Co OR (CI)	Contralateral Ca/Co OR (CI)
Acoustic neuroma (n=243)			
Mobile phone, > 1 year latency	130/900 1.7 1.2-2.3	80/374 1.8 1.2-2.6	48/308 1.4 0.9-2.1
>10 year latency	20/99 2.9 1.6-5.5	13/45 3.0 1.4-6.2	6/29 2.4 0.9-6.3
Cordless phone, > 1 year latency	96/701 1.5 1.04-2.0	67/309 1.7 1.2-2.5	28/235 1.1 0.7-1.7
>10 year latency	4/45 1.3 0.4-3.8	3/15 2.3 0.6-8.8	1/20 0.5 0.1-4.0
Meningioma (n=916)			
Mobile phone, > 1 year latency	347/900 1.1 0.9-1.3	167/374 1.3 1.01-1.7	125/308 1.1 0.8-1.4
>10 year latency	38/99 1.5 0.98-2.4	18/45 1.6 0.9-2.9	12/29 1.6 0.7-3.3
Cordless phone, > 1 year latency	294/701 1.1 0.9-1.4	134/309 1.2 0.9-1.6	101/235 1.1 0.8-1.5
>10 year latency	23/45 1.8 1.01-3.2	11/15 3.0 1.3-7.2	7/20 1.1 0.5-2.9
Other benign brain tumours (n=96)			
Mobile phone, > 1 year latency	49/900 1.5 0.9-2.5	11/374 1.4 0.5-3.8	12/308 2.1 0.8-5.3
>10 year latency	7/99 1.8 0.7-4.9	4/45 4.7 1.1-21	1/29 2.6 0.2-30
Cordless phone, > 1 year latency	34/701 1.5 0.8-2.5	8/309 1.5 0.5-4.3	9/235 2.0 0.7-5.5
>10 year latency	1/45 1.3 0.1-12	1/15 9.2 0.4-197	0/20 -

Table 3. Odds ratio (OR) and 95 % confidence interval (CI) for astrocytoma and acoustic neuroma in different age groups. Numbers of exposed cases (Ca) and controls (Co) are given. Adjustment was made for age, sex, SEI, and year of diagnosis.

Age at first exposure/ Type of telephone	Astrocytoma Ca/Co OR (CI)	Acoustic neuroma Ca/Co OR (CI)
All ages, > 1 year latency		
Mobile phone	346/900 1.4 1.1-1.7	130/900 1.7 1.2-2.3
Cordless phone	261/701 1.4 1.1-1.8	96/701 1.5 1.04-2.0
<20, > 1 year latency		
Mobile phone	15/14 5.2 2.2-12	5/14 5.0 1.5-16
Cordless phone	14/16 4.4 1.9-10	1/16 0.7 0.1-5.9
20-49, > 1 year latency		
Mobile phone	208/555 1.5 1.1-2.0	86/555 2.0 1.3-2.9
Cordless phone	138/416 1.3 0.98-1.8	65/416 1.7 1.1-2.5
50-80, > 1 year latency		
Mobile phone	123/331 1.3 0.97-1.7	39/331 1.4 0.9-2.2
Cordless phone	109/269 1.5 1.1-2.0	30/269 1.3 0.8-2.1

Table 4. Odds ratios (ORs) and 95 % confidence intervals (CIs) for meta-analysis of six case-control studies on glioma, four on acoustic neuroma and five on meningioma using ≥ 10 year latency period. Numbers of exposed cases (Ca) and controls (Co) are given. Note that ipsilateral use was defined as in the different published studies, for further details, see Hardell et al (2009).

	Total			**Ipsilateral**			**Contralateral**		
	No. of Ca/Co	OR	95 % CI	No. of Ca/Co	OR	95 % CI	No. of Ca/Co	OR	95 % CI
Glioma	233/330	1.3	1.1 – 1.6	118/145	1.9	1.4 – 2.4	93/150	1.2	0.9 – 1.7
Acoustic neuroma	67/311	1.3	0.97 – 1.9	41/152	1.6	1.1 – 2.4	26/134	1.2	0.8 – 1.9
Meningioma	116/320	1.1	0.8 – 1.4	48/141	1.3	0.9 – 1.8	36/146	0.8	0.5 – 1.3