

Case-Control Study on Cellular and Cordless Telephones and the Risk for Acoustic Neuroma or Meningioma in Patients Diagnosed 2000–2003

Lennart Hardell^a Michael Carlberg^b Kjell Hansson Mild^c

^aDepartment of Oncology, University Hospital, and Department of Natural Sciences, Örebro University,

^bDepartment of Oncology, University Hospital, and ^cNational Institute for Working Life and Department of Natural Sciences, Örebro University, Örebro, Sweden

Key Words

Microwaves · Digital phones · Analogue phones · Benign brain tumors · Cordless phones

Abstract

We performed a case-control study on the use of cellular and cordless telephones and the risk for brain tumors. We report the results for benign brain tumors with data from 413 cases (89% response rate), 305 with meningioma, 84 with acoustic neuroma, 24 with other types and 692 controls (84% response rate). For meningioma, analogue phones yielded odds ratio (OR) = 1.7, 95% confidence interval (CI) = 0.97–3.0, increasing to OR = 2.1, 95% CI = 1.1–4.3 with a >10-year latency period. Also digital cellular phones and cordless phones increased the risk to some extent. For acoustic neuroma, analogue phones gave OR = 4.2, 95% CI = 1.8–10 increasing to OR = 8.4, 95% CI = 1.6–45 with a >15-year latency period, but based on low numbers. Digital phones yielded OR = 2.0, 95% CI = 1.05–3.8, whereas for cordless phones OR was not significantly increased. In the multivariate analysis, analogue phones represented a significant risk factor for acoustic neuroma.

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Introduction

During calls with cellular or cordless phones, the brain is exposed to microwaves in the range of 400–2,000 MHz. The temporal area is a part of the brain with the highest exposure due to physical properties of the phone. However, depending on the site of the antenna and how the phone is held other parts of the brain may also have substantial exposure.

Acoustic neuroma is a benign tumor of the 8th cranial nerve. It develops in an area with higher exposure to microwaves from cellular and cordless phones than other parts of the brain and may thus be a signal tumor for a carcinogenic potential of microwaves. In previous epidemiological studies, we found an association between cellular telephone use and brain tumors [1–6]. The most increased risk was found for acoustic neuroma. Regarding salivary gland tumors, we found no association, although the parotid gland is located in an area with high exposure to microwaves from cellular telephones compared with other anatomical sites [7]. These and other results on this topic have been recently reviewed elsewhere [8–10] and are not further discussed here.

In Sweden, the analogue Nordic Mobile Telephone System was introduced in 1981, operating at 450 MHz, often in a car with fixed external antenna, but from 1984

the first portable analogue phones were available. The Nordic Mobile Telephone System 900 MHz system was used in Sweden between 1986 and 2000. Global System for Mobile Communication is a digital system that was introduced in 1991 and since the late 1990s has become the most popular phone system. Desktop cordless telephones are used in Sweden since 1988. First, the analogue system in the 800–900 MHz RF range was available on the market, but now usually digital cordless telephones that operate at 1,900 MHz are used.

There is a variation of the specific absorption rate (SAR) between the different types of cellular telephones. However, this information is not easily available since the subjects cannot mostly remember the brand names of the cellular phones used over time. Moreover, information on SAR is usually lacking from the manufactures.

We have now further investigated use of cellular and cordless telephones and the association with brain tumors by extending our previous study with more study years. We used the same study methods including the same questionnaire as in our previous study. The ethical committees approved the study. The results for use of cellular and cordless telephones and the risk for benign brain tumors are presented here. Results for malignant tumors will be presented separately.

Materials and Methods

Cases were recruited during the time period July 1, 2000 until December 31, 2003. Both men and women aged 20–80 years at the time of diagnosis were included. They were inhabitants in the Uppsala/Örebro and Linköping medical regions in Sweden. All had a histopathological diagnosis that had been reported to the regional cancer registries in Uppsala and Linköping. These registries sent information to our study group as soon as a new case was reported. Permission to include the patient in the study was asked for from the treating physician. Only living patients were included.

Control subjects were identified from the national population registry covering the whole population. The controls were aged 20–80 years and lived in the same geographical area as the cases, i.e. Uppsala/Örebro and Linköping medical regions. They were matched for age and selected at random in 5-year age groups according to the number of cases in the different age groups. One control was identified to each finally included case. Each study subject was given a unique ID number that did not show if it was a case or a control.

Assessment of Exposure

Exposures to cellular and cordless phones were assessed by a questionnaire including also exposure to certain agents and lifetime work history, whereby socioeconomic index (SEI) was assessed since adjustment was made for the SEI code in the statistical analyses. The answers were supplemented over the phone by a trained

interviewer using a written protocol. In the assessment of exposure, case or control status was not disclosed to the interviewers. All subjects were identified by a unique ID number.

The median time from the date of diagnosis until sending the questionnaire was 79 days. This lag time included reporting from the cancer registry and obtaining permission from the treating physician to contact the patient. This time between diagnosis and interview is of potential benefit compared with bedside interview since the patient has been informed about the diagnosis and further medical care. The situation is also more relaxed at home than in hospitals and is similar to the situation of the controls.

Mean number of daily calls and minutes were asked for and used to calculate the cumulative use in hours from the first year of use up to the year before diagnosis. Thereby, the same year, i.e. year of diagnosis, was used for the matched control as for the corresponding case. Those who started their first use of a mobile or cordless phone within 1 year prior to diagnosis were regarded as unexposed.

If the cellular telephone had been used in a car with fixed external antenna, such time was disregarded. Similarly, use of a hands-free device with an earpiece was excluded in the calculation of total number of hours. We also assessed information on the ear most frequently used during calls with cellular and cordless telephones over the years, or if both ears were equally used. It was important to find out which ear was used during the whole time since some subjects might have changed the habit, e.g. due to the brain tumor.

Since it was important to differentiate between analogue and digital cellular telephones, we checked the first part of the phone number (prefix). Thus, all analogue phone numbers started with 010 and digital with 07. If the first year in which the subject had reported use of a cellular or cordless phone was apparently incorrect, i.e. before the respective phone was on the market, this was corrected during the interviews and coding of exposure.

In addition to phone interviews, an additional letter was sent to all cases reporting regular use of a fixed antenna in a car in order to exclude that the question was misunderstood. Also, the ear mostly used during phone calls was checked by an additional letter to get information on the habit over the years, possible change of ear, to what extent each ear had been used, etc.

Histopathology was obtained from the cancer registry and if missing from pathology departments. For many cases, information on tumor localization was also available in the Cancer Registry report. If necessary, copies of reports of neuroradiology investigations were requested from radiology units at different hospitals in order to get correct diagnosis and tumor localization. This was done after informed consent from the cases. Coding of anatomical area for the tumor was done without knowing if the subject was exposed to cellular or cordless phones. All information was coded by two independent persons, registered into data files and analyzed twice with same results, thus avoiding bias during that process. Thereby only the ID number was used. This procedure was the same as in our previous study and has been discussed by us [3].

Statistical Methods

Unconditional logistic regression analysis was used to calculate odds ratios (OR) and 95% confidence intervals (CI), (Stata/SE 8.2 for Windows; StataCorp, College Station, Tex., USA). Thereby, also incomplete pairs could be included in the analysis. The

material was divided into two groups, exposed and unexposed. The exposed cases and controls were further divided according to use of analogue or digital cellular phones and cordless phones. Note that a person may have been using more than one type of telephone. The unexposed group consisted of cases and controls without exposure to cellular or cordless telephones. Adjustment was made for sex, age, SEI code and year of diagnosis. For the controls, the same year was used as for the corresponding cases. Latency (tumor induction period) was analyzed using three time periods, >1–5 years, >5–10 years and >10 years since the first use of a cellular or cordless telephone until tumor diagnosis. In the dose-response calculations, the median number of cumulative use in hours among controls was used as a cut-off. Note that overall results for all latency groups were calculated in one analysis whereas dose-response was analyzed separately for each category.

Results

In total, 1,168 cases were reported from the two cancer registries. Of these, 348 were excluded since they did not meet the study criteria (table 1). Of the excluded cases, 205 had died, 18 with a benign brain tumor, and were thus not included. The study thus included 820 cases with benign or malignant brain tumor and 820 controls. Of the 462 included cases with benign brain tumor 413 (89%, 128 men, 285 women) participated. Regarding the 820 controls 692 (84%) (292 men, 400 women) answered the questionnaire. The mean age was 56 years for cases and 55 years for controls. Results for benign brain tumors are given below.

No use of cellular or cordless phones was reported by 123 (29.8 %) cases and 233 (33.7 %) controls. In table 2, overall results are presented. No separate calculation was made for 24 cases with other types of benign tumors than acoustic neuroma or meningioma due to low numbers. Use of analogue telephones yielded OR = 2.4, 95% CI = 1.5–3.9. The risk increased further with longer latency periods, for >15 years OR = 4.3, 95% CI = 1.7–11 (12 cases, 12 controls).

Digital cellular telephones yielded OR = 1.5, 95% CI = 1.1–2.1 and with the >10-year latency period OR = 2.0, 95% CI = 0.9–4.5. Use of cordless telephones gave OR = 1.5, 95% CI = 1.1–2.0, but did not increase with latency period.

Most of the cases were diagnosed with meningioma, 76 men and 229 women. Regarding analogue phones with the >1-year latency period, OR = 1.7, 95% CI = 0.97–3.0 was calculated, increasing to OR = 2.1, 95% CI = 1.1–4.3 with the >10-year latency period. Using the >1-year latency period, digital phones yielded in the highest exposure category (>64 h) OR = 1.7, 95% CI =

Table 1. Number of cases aged 20–80 years reported from the cancer registries

| | |
|--|-------|
| Total reported | 1,168 |
| Metastasis or other localization than brain | 56 |
| Wrong year for diagnosis | 15 |
| Histopathology missing | 1 |
| Deceased | 205 |
| Benign | 18 |
| Malignant | 187 |
| Astrocytoma | 169 |
| Other | 18 |
| Refused by treating physician to be included | 46 |
| Not capable to be included for medical reasons as reported by case or relative | 23 |
| Not included due to other language | 2 |
| Total included | 820 |
| Malignant ¹ | 359 |
| Benign ¹ | 462 |
| Refused to participate | 91 |
| Malignant | 42 |
| Benign | 49 |
| Included in analysis | 729 |
| Malignant ¹ | 317 |
| Benign ¹ | 413 |

¹ One case had both a malignant and a benign tumor.

1.1–2.6 and cordless phones (>243 h) OR = 1.7, 95% CI = 1.1–2.6.

Regarding acoustic neuroma (39 men, 45 women) both cellular and cordless telephones increased the risk. For analogue phones, OR was significantly increased for latency periods of >1–5 and >5–10 years. Lower OR was calculated for the >10-year latency period, but most of all these results were based on low numbers. For the >15-year latency period OR = 8.4, 95% CI = 1.6–45 (4 cases, 12 controls) was calculated. For the >1-year latency period, the calculation for use of digital phones showed OR = 2.0, 95% CI = 1.05–3.8, increasing to OR = 2.7, 95% CI = 1.3–5.7 using the >5- to 10-year latency period. A dose-response effect was seen in the overall results and in the >5- to 10-year latency group. Cordless phones yielded somewhat increased but not significant risk.

In table 3, OR and 95% CI are presented for different tumor localizations. Since all cases with acoustic neuroma (n = 84) were located in the temporal area, they were excluded.

Increased risk was found for other tumors, mostly meningioma (n = 81) located in the temporal area for all phone types. Using the >10-year latency period, OR in-

Table 2. Number of exposed cases (Ca) with benign brain tumor and controls (Co), OR and 95% CI for use of cellular or cordless telephones

| | >1- to 5-year latency | | >5- to 10-year latency | | >10-year latency | | Total, >1-year latency | |
|--|-----------------------|---------------|------------------------|---------------|------------------|---------------|------------------------|---------------|
| | Ca/Co | OR, CI | Ca/Co | OR, CI | Ca/Co | OR, CI | Ca/Co | OR, CI |
| Benign (n = 413, 123 unexposed) | | | | | | | | |
| Analogue | 4/3 | 3.9, 0.8–19 | 28/36 | 2.3, 1.2–4.2 | 30/40 | 2.4, 1.3–4.4 | 62/79 | 2.4, 1.5–3.9 |
| ≤80 h | 4/3 | 3.9, 0.8–19 | 10/24 | 1.1, 0.5–2.6 | 12/13 | 3.3, 1.3–8.2 | 26/40 | 1.9, 1.02–3.4 |
| >80 h | 0/0 | – | 18/12 | 5.6, 2.3–13 | 18/27 | 2.6, 1.2–5.4 | 36/39 | 3.1, 1.7–5.6 |
| Digital | 131/214 | 1.4, 0.98–2.0 | 74/111 | 1.8, 1.2–2.7 | 13/18 | 2.0, 0.9–4.5 | 218/343 | 1.5, 1.1–2.1 |
| ≤64 h | 79/139 | 1.3, 0.9–1.9 | 29/44 | 1.6, 0.9–2.8 | 0/0 | – | 108/183 | 1.3, 0.9–1.9 |
| >64 h | 52/75 | 1.9, 1.2–3.1 | 45/67 | 2.2, 1.3–3.7 | 13/18 | 2.0, 0.9–4.5 | 110/160 | 1.9, 1.3–2.8 |
| Cordless | 122/170 | 1.6, 1.1–2.2 | 57/100 | 1.3, 0.8–2.0 | 21/35 | 1.5, 0.8–2.8 | 200/305 | 1.5, 1.1–2.0 |
| ≤243 h | 72/110 | 1.5, 0.98–2.2 | 11/37 | 0.7, 0.3–1.4 | 3/12 | 1.1, 0.3–4.1 | 86/159 | 1.2, 0.8–1.7 |
| >243 h | 50/60 | 2.0, 1.2–3.3 | 46/63 | 1.9, 1.1–3.1 | 18/23 | 2.1, 1.02–4.3 | 114/146 | 1.9, 1.3–2.7 |
| Meningioma (n = 305, 103 unexposed) | | | | | | | | |
| Analogue | 1/3 | 1.2, 0.1–12 | 14/36 | 1.4, 0.7–2.8 | 20/40 | 2.1, 1.1–4.3 | 35/79 | 1.7, 0.97–3.0 |
| ≤80 h | 1/3 | 1.2, 0.1–12 | 6/24 | 0.8, 0.3–2.2 | 8/13 | 2.9, 1.1–8.1 | 15/40 | 1.4, 0.7–2.7 |
| >80 h | 0/0 | – | 8/12 | 2.8, 0.98–7.8 | 12/27 | 2.3, 1.01–5.4 | 20/39 | 2.2, 1.1–4.3 |
| Digital | 96/214 | 1.2, 0.8–1.8 | 47/111 | 1.4, 0.9–2.3 | 8/18 | 1.5, 0.6–3.9 | 151/343 | 1.3, 0.9–1.9 |
| ≤64 h | 57/139 | 1.1, 0.7–1.7 | 20/44 | 1.3, 0.7–2.5 | 0/0 | – | 77/183 | 1.1, 0.8–1.7 |
| >64 h | 39/75 | 1.8, 1.1–3.0 | 27/67 | 1.6, 0.9–3.0 | 8/18 | 1.5, 0.6–3.9 | 74/160 | 1.7, 1.1–2.6 |
| Cordless | 81/170 | 1.3, 0.9–1.9 | 40/100 | 1.1, 0.7–1.8 | 19/35 | 1.9, 0.97–3.6 | 140/305 | 1.3, 0.9–1.9 |
| ≤243 h | 48/110 | 1.2, 0.8–1.9 | 8/37 | 0.6, 0.3–1.4 | 3/12 | 1.2, 0.3–4.9 | 59/159 | 1.0, 0.7–1.6 |
| >243 h | 33/60 | 1.7, 0.98–3.0 | 32/63 | 1.6, 0.9–2.8 | 16/23 | 2.3, 1.1–4.9 | 81/146 | 1.7, 1.1–2.6 |
| Acoustic neuroma (n = 84, 18 unexposed) | | | | | | | | |
| Analogue | 2/3 | 9.9, 1.4–69 | 11/36 | 5.1, 1.9–14 | 7/40 | 2.6, 0.9–8.0 | 20/79 | 4.2, 1.8–10 |
| ≤80 h | 2/3 | 9.9, 1.4–69 | 3/24 | 2.3, 0.6–9.0 | 2/13 | 2.3, 0.4–14 | 7/40 | 3.0, 1.1–8.6 |
| >80 h | 0/0 | – | 8/12 | 1.8, 4.6–71 | 5/27 | 3.1, 0.8–12 | 13/39 | 6.0, 2.2–17 |
| Digital | 29/214 | 1.7, 0.9–3.5 | 23/111 | 2.7, 1.3–5.7 | 1/18 | 0.8, 0.1–6.7 | 53/343 | 2.0, 1.05–3.8 |
| ≤64 h | 18/139 | 1.7, 0.8–3.7 | 5/44 | 1.7, 0.6–4.9 | 0/0 | – | 23/183 | 1.7, 0.8–3.4 |
| >64 h | 11/75 | 1.9, 0.7–4.7 | 18/67 | 5.2, 2.0–14 | 1/18 | 0.8, 0.1–6.7 | 30/160 | 2.5, 1.2–5.2 |
| Cordless | 31/170 | 1.8, 0.9–3.6 | 13/100 | 1.4, 0.6–3.2 | 1/35 | 0.3, 0.03–2.2 | 45/305 | 1.5, 0.8–2.9 |
| ≤243 h | 18/110 | 1.8, 0.9–3.8 | 3/37 | 1.1, 0.3–4.2 | 0/12 | – | 21/159 | 1.4, 0.7–2.9 |
| >243 h | 13/60 | 2.2, 0.9–5.4 | 10/63 | 2.0, 0.8–5.3 | 1/23 | 0.8, 0.1–6.8 | 24/146 | 1.7, 0.8–3.5 |

Unconditional logistic regression analysis adjusted for age, sex, SEI and year of diagnosis was used. In the dose-response calculations, median number of cumulative use in hours among controls was used as cut-off.

creased for analogue phones to 5.7, 95% CI = 1.7–19, digital cellular phones gave OR = 5.3, 95% CI = 1.5–19 and cordless phones OR = 5.6, 95% CI = 2.1–15. It should be noted that some of the calculations were based on low numbers. All these cases with the >10-year latency period had meningioma.

In table 4, results for the >1-year latency period are presented for anatomical tumor area in relation to the ear that had mostly been used during phone calls, or both ears used equally often.

For meningioma, no clear pattern of laterality of tumor site in relation to ear used during phone calls was found. However, for acoustic neuroma highest OR was found for

ipsilateral use of the phone, for analogue phones OR = 5.1, 95% CI = 1.9–14, digital phones OR = 2.9, 95% CI = 1.4–6.1 and cordless phones OR = 2.4, 95% CI = 1.1–5.1. Increased risk was also found for contralateral and equal ipsi- and contralateral use that may be explained by the fact that patients with acoustic neuroma may switch the ear for phone calls due to tumor symptoms.

Table 5 presents results for multivariate analysis. The risk was significantly increased for acoustic neuroma and use of analogue phones with OR = 2.1, 95% CI = 1.1–3.8 (>1-year latency period). Somewhat increased risk was also found for meningioma, although not significantly so.

Table 3. Number of exposed cases (Ca) with benign brain tumor and controls (Co), OR and 95% CI for use of cellular or cordless telephones for different tumor localizations

| | >1- to 5-year latency | | >5- to 10-year latency | | >10-year latency | | Total, >1-year latency | |
|-------------------------------------|-----------------------|--------------|------------------------|--------------|------------------|--------------|------------------------|--------------|
| | Ca/Co | OR, CI | Ca/Co | OR, CI | Ca/Co | OR, CI | Ca/Co | OR, CI |
| Temporal (n = 84, 18 unexposed) | | | | | | | | |
| Analogue | 0/3 | – | 5/36 | 3.3, 0.99–11 | 7/40 | 5.7, 1.7–19 | 12/79 | 4.1, 1.5–11 |
| Digital | 33/214 | 2.8, 1.4–5.8 | 16/111 | 3.3, 1.5–7.6 | 4/18 | 5.3, 1.5–19 | 53/343 | 3.1, 1.6–6.1 |
| Cordless | 24/170 | 2.3, 1.1–4.6 | 11/100 | 1.8, 0.8–4.3 | 9/35 | 5.6, 2.1–15 | 44/305 | 2.4, 1.3–4.7 |
| Frontal (n = 111, 42 unexposed) | | | | | | | | |
| Analogue | 0/3 | – | 4/36 | 1.0, 0.3–3.2 | 6/40 | 1.8, 0.6–5.2 | 10/79 | 1.3, 0.5–3.0 |
| Digital | 28/214 | 0.9, 0.5–1.6 | 16/111 | 1.2, 0.6–2.4 | 1/18 | 0.4, 0.1–3.3 | 45/343 | 0.9, 0.6–1.6 |
| Cordless | 37/170 | 1.5, 0.9–2.6 | 11/100 | 0.8, 0.4–1.8 | 7/35 | 2.2, 0.8–5.7 | 55/305 | 1.4, 0.8–2.2 |
| Other parts (n = 134, 45 unexposed) | | | | | | | | |
| Analogue | 2/3 | 5.0, 0.7–33 | 8/36 | 1.5, 0.6–3.7 | 10/40 | 1.9, 0.8–4.7 | 20/79 | 1.8, 0.9–3.7 |
| Digital | 41/214 | 1.2, 0.7–2.0 | 19/111 | 1.2, 0.6–2.3 | 7/18 | 2.9, 1.1–8.0 | 67/343 | 1.3, 0.8–2.1 |
| Cordless | 30/170 | 1.0, 0.6–1.8 | 22/100 | 1.3, 0.7–2.4 | 4/35 | 0.7, 0.2–2.3 | 56/305 | 1.1, 0.7–1.8 |

Unconditional logistic regression analysis adjusted for age, sex, SEI and year of diagnosis was used. Cases with acoustic neuroma (n = 84) were excluded.

Table 4. Number of exposed cases (Ca) with benign brain tumor and controls (Co), OR and 95% CI for use of cellular or cordless telephones for tumor localizations in relation to the ear used during phone calls

| Localization/ type of telephone | All | | Ipsilateral | | Contralateral | | Ipsi/contralateral | |
|------------------------------------|---------|---------------|-------------|---------------|---------------|---------------|--------------------|--------------|
| | Ca/Co | OR, CI | Ca/Co | OR, CI | Ca/Co | OR, CI | Ca/Co | OR, CI |
| Benign | | | | | | | | |
| Analogue phone | 62/79 | 2.4, 1.5–3.9 | 26/25 | 3.3, 1.6–6.8 | 21/28 | 3.1, 1.5–6.7 | 7/14 | 1.9, 0.7–5.4 |
| Digital phone | 218/343 | 1.5, 1.1–2.1 | 88/108 | 2.0, 1.3–3.1 | 82/124 | 1.6, 1.1–2.5 | 27/41 | 2.1, 1.1–4.1 |
| Cordless phone | 200/305 | 1.5, 1.1–2.0 | 80/97 | 2.0, 1.3–3.1 | 73/99 | 1.6, 1.01–2.5 | 21/43 | 1.2, 0.6–2.4 |
| Meningioma | | | | | | | | |
| Analogue phone | 35/79 | 1.7, 0.97–3.0 | 10/25 | 1.6, 0.7–3.9 | 14/28 | 2.6, 1.1–6.0 | 4/14 | 1.4, 0.4–4.8 |
| Digital phone | 151/343 | 1.3, 0.9–1.9 | 54/108 | 1.5, 0.9–2.5 | 62/124 | 1.5, 0.9–2.3 | 17/41 | 1.7, 0.8–3.7 |
| Cordless phone | 140/305 | 1.3, 0.9–1.9 | 51/97 | 1.6, 0.97–2.6 | 55/99 | 1.5, 0.9–2.4 | 12/43 | 0.9, 0.4–2.0 |
| Acoustic neuroma | | | | | | | | |
| Analogue phone | 20/79 | 4.2, 1.8–10 | 12/25 | 5.1, 1.9–14 | 5/28 | 4.9, 1.2–21 | 3/14 | 3.9, 0.8–19 |
| Digital phone | 53/343 | 2.0, 1.05–3.8 | 29/108 | 2.9, 1.4–6.1 | 15/124 | 1.6, 0.7–3.7 | 9/41 | 3.5, 1.1–11 |
| Cordless phone | 45/305 | 1.5, 0.8–2.9 | 25/97 | 2.4, 1.1–5.1 | 13/99 | 1.4, 0.6–3.2 | 7/43 | 2.1, 0.7–6.4 |

Ipsilateral = Same side for tumor and phone; contralateral = opposite sides; ipsi/contralateral = both ears used equally often. Unconditional logistic regression analysis adjusted for age, sex, SEI and year of diagnosis was used. Note that tumor site was missing for some cases and the matched control was excluded as well as controls with missing corresponding case.

We also calculated OR and CI for different phone types used alone, or in different combinations. Thereby the >1-year latency period was used as presented in table 6. In the calculations, highest ORs were found for use of analogue phones in any combination.

Discussion

In two previous studies, we have found an increased risk for brain tumors associated with cellular telephone use [1–6]. The risk was highest on the side of the brain

Table 5. Unconditional logistic regression multivariate analysis adjusted for age, sex, SEI and year of diagnosis

| | >1- to 5-year latency | | >5- to 10-year latency | | >10-year latency | | Total, >1-year latency | |
|-------------------------|-----------------------|---------------|------------------------|---------------|------------------|---------------|------------------------|--------------|
| | Ca/Co | OR, CI | Ca/Co | OR, CI | Ca/Co | OR, CI | Ca/Co | OR, CI |
| Benign | | | | | | | | |
| Analogue | 4/3 | 2.4, 0.5–11 | 28/36 | 1.6, 0.9–2.7 | 30/40 | 1.7, 0.99–2.8 | 62/79 | 1.7, 1.1–2.5 |
| Digital | 131/214 | 1.0, 0.8–1.4 | 74/111 | 1.4, 0.99–2.0 | 13/18 | 1.4, 0.6–2.9 | 218/343 | 1.2, 0.9–1.6 |
| Cordless | 122/170 | 1.3, 0.96–1.7 | 57/100 | 0.9, 0.6–1.3 | 21/35 | 1.1, 0.6–1.9 | 200/305 | 1.2, 0.9–1.5 |
| Meningioma | | | | | | | | |
| Analogue | 1/3 | 0.9, 0.1–9.0 | 14/36 | 1.1, 0.6–2.1 | 20/40 | 1.8, 0.96–3.2 | 35/79 | 1.4, 0.9–2.2 |
| Digital | 96/214 | 1.1, 0.8–1.5 | 47/111 | 1.3, 0.9–1.9 | 8/18 | 1.1, 0.5–2.7 | 151/343 | 1.2, 0.9–1.6 |
| Cordless | 81/170 | 1.1, 0.8–1.5 | 40/100 | 0.9, 0.6–1.3 | 19/35 | 1.5, 0.8–2.7 | 140/305 | 1.1, 0.8–1.5 |
| Acoustic neuroma | | | | | | | | |
| Analogue | 2/3 | 4.2, 0.7–26 | 11/36 | 2.4, 1.1–5.1 | 7/40 | 1.5, 0.6–3.6 | 20/79 | 2.1, 1.1–3.8 |
| Digital | 29/214 | 1.0, 0.6–1.6 | 23/111 | 2.0, 1.1–3.5 | 1/18 | 0.5, 0.1–4.2 | 53/343 | 1.4, 0.8–2.4 |
| Cordless | 31/170 | 1.6, 0.99–2.7 | 13/100 | 0.9, 0.5–1.7 | 1/35 | 0.2, 0.03–1.5 | 45/305 | 1.2, 0.8–2.0 |

Table 6. Number of exposed cases (Ca) with benign brain tumor and controls (Co), OR and 95% CI for use of cellular or cordless telephones for different combinations of phone use

| Combination | Benign, all | | Meningioma | | Acoustic neuroma | |
|-------------------------------|-------------|---------------|------------|----------------|------------------|---------------|
| | Ca/Co | OR, CI | Ca/Co | OR, CI | Ca/Co | OR, CI |
| Analogue only | 3/7 | 1.1, 0.3–4.6 | 1/7 | 0.4, 0.04–3.1 | 1/7 | 3.1, 0.3–30 |
| Digital only | 69/117 | 1.4, 0.9–2.1 | 50/117 | 1.2, 0.7–1.8 | 15/117 | 2.1, 0.9–4.7 |
| Cordless only | 63/103 | 1.3, 0.8–1.9 | 48/103 | 1.2, 0.7–1.9 | 10/103 | 1.0, 0.4–2.5 |
| Analogue + digital | 53/66 | 2.8, 1.6–4.7 | 32/66 | 2.1, 1.2–3.9 | 17/66 | 5.0, 1.9–13 |
| Analogue + cordless | 41/42 | 3.5, 1.9–6.4 | 23/42 | 2.4, 1.2–4.8 | 14/42 | 7.0, 2.4–20 |
| Digital + cordless | 131/196 | 1.7, 1.2–2.5 | 90/196 | 1.5, 0.999–2.3 | 33/196 | 2.0, 0.98–4.3 |
| Analogue + digital + cordless | 35/36 | 3.7, 1.9–6.9 | 21/36 | 2.8, 1.3–5.6 | 12/36 | 8.4, 2.7–27 |
| Total, any combination | 290/459 | 1.4, 1.03–1.9 | 202/459 | 1.2, 0.9–1.6 | 66/459 | 1.6, 0.9–2.9 |

Unconditional logistic regression analysis adjusted for age, sex, SEI and year of diagnosis was used.

where the cellular phone had been used and increased with tumor induction period, which is of biological relevance. Regarding benign brain tumors, significantly increased risk was found for acoustic neuroma but not for meningioma [5, 6].

Reporting new cancer cases to the Swedish cancer registry is compulsory. Also certain benign diseases, such as benign brain tumors, are reported. As soon as the histopathological diagnosis is obtained, the respective pathological departments send a report to the local cancer registry in the five medical regions in Sweden. In addition, the treating physician makes a clinical report. Thus, a high reporting frequency is obtained with good coverage

of all new cases, and no selection bias as to reporting exists.

Cases were reported in a consecutive way to us from the two cancer registries in both medical regions, and we have no indication of selection bias in this respect. Only 18 of the cases that died before interview had a benign tumor, and exclusion of these cases may hardly bias the results.

For inclusion, it was necessary to have histopathological verification of the diagnosis. If information was unclear or missing in the cancer registry, we obtained copies of records from the pathology and radiology departments. It is important to carefully assess the medical coding of

Table 7. Number of cases in different categories of latency period and cumulative use of cellular telephones in epidemiological studies

| Study | ≥ 5 years | >10 years | >500 h | >2,000 h |
|--|---|---|--|---|
| Hardell et al. [3–6 and to be published], 1997–2003 | analogue 308 digital 365 cordless 420 cellular 566 | analogue 138 digital 32 cordless 61 cellular 159 | analogue 74 digital 135 cordless 283 cellular 189 | analogue 27 digital 29 cordless 82 cellular 54 |
| Inskip et al. [13], USA, 1994–1998 | cellular 22 (≥ 5 years) | not given | 18 | not given |
| Muscat et al. [12], USA, 1994–1998 | cellular 17 (≥ 4 years) | not given | 14 (≥ 480 h) | not given |
| Johansen et al. [15], Denmark, 1982–1995 (users) | cellular 24 (≥ 5 years) digital 9 (≥ 3 years) | not given | not given | not given |
| Christensen et al. [17], Denmark, 2000–2002 (acoustic neuroma) | cellular 19 | cellular 2 | 8 (>654 h) | not given |
| Auvinen et al. [14], Finland, 1996 | analogue 17 digital 1 (>2 years) | not given | not given | not given |
| Lönn et al. [19], 1999–2002 (acoustic neuroma) | analogue 27 digital 29 cellular 44 | analogue 14 digital 0 cellular 14 (≥ 10 years) | cellular 21 (≥ 450 h) | not given |
| Lönn et al. [22], 2000–2002 (glioma) | analogue 50 digital 83 cellular 100 | analogue 25 digital 0 cellular 25 (≥ 10 years) | cellular 42 (≥ 500 h) | not given |
| Lönn et al. [22], 2000–2002 (meningioma) | analogue 23 digital 43 cellular 52 | analogue 12 digital 0 cellular 12 (≥ 10 years) | cellular 25 (≥ 500 h) | not given |

Note that only the Hardell et al. studies have information on cordless telephone use. The term ‘cellular’ is used for analogue and/or digital cellular phones.

brain tumors in the cancer registry, as also shown in our previous report [3].

All exposure was assessed and coded in a blinded manner as to case or control status so as to avoid observational bias. Misclassification of exposure may occur if cases recall exposure different to controls. However, we found a different risk pattern for meningioma and acoustic neuroma, and recall bias would not be dependent on tumor type. Furthermore, the more recent findings on acoustic neuroma had not been presented during the study period [see 19]. Cordless telephones have not been discussed as a risk factor for brain tumors in the population, so also the results for that phone type indicate that recall bias may not explain the results.

One option to validate use of phones would be to get information on billing records from the phone compa-

nies. However, phone companies have been reluctant to release such information for business reasons. Furthermore, several persons may use corporate as well as personal phones, pay-as-you-talk cards are very common and a personal registration of the phone may not exist; the value of such an approach is thus limited. Also no information would be obtained on received calls.

Our main finding was a significantly increased risk for acoustic neuroma and use of analogue cellular telephones. OR increased with increasing number of hours for use. The highest risk was found for the >15-year latency period, although this result is based on low numbers and must be interpreted with caution. In a multivariate analysis, use of analogue phones persisted as a significant risk factor for acoustic neuroma. Regarding digital cellular telephones, significantly increased risk was only found in

the >5- to 10-year latency period, and the biological relevance of that finding is unclear. Clearly, use of cordless phones did not increase the risk for acoustic neuroma.

Meningioma was more common among women than men as would be expected [11]. We found somewhat increased risk for the studied phone types (table 2). This finding was supported in the analysis of the risk for tumors in different anatomical areas of the brain. Thus, significantly increased risk was found for tumors in the temporal area but not in other parts of the brain. Of the 84 cases with this type of tumor, 81 had meningioma. It should be noted that all cases with acoustic neuroma (n = 84) were excluded from this calculation since all were located in the temporal area. One case had both acoustic neuroma and a malignant brain tumor in other part of the brain, here included among the acoustic neuroma cases.

However, in the calculations of laterality of tumor and phone use no clear pattern was found for meningioma. Furthermore, in the multivariate analysis no phone type yielded significantly increased risk for meningioma. Thus, no clear association was found and the results deserve further studies in the future with a longer follow-up period.

Since the inclusion period of cases was between July 1, 2000 and December 31, 2003 all phone types had been on the market for more than 10 years. Regarding acoustic neuroma, the median latency periods were: 9.5 years for analogue phones, 5 years for digital cellular phones and 4 years for cordless phones. Regarding meningioma, the median latency periods were 11 years for analogue phones, 4 years for digital cellular phones and 5 years for cordless phones.

Epidemiological research on the risk of brain tumors and use of cellular and cordless phones is limited. Regarding cellular telephones, few case-control studies and only one cohort study exist. Two hospital-based case-control studies from USA did not find an increased risk [12, 13]. However, both were inconclusive because of short duration of use and short latency periods. In a registry-based case-control study from Finland, a significantly increased risk was found for all brain tumors and glioma [14]. Omission of corporate subscriptions, short duration of use and possible exposure misclassification gave limited evidence of an association. A Danish retrospective cohort study on private subscribers was inconclusive due to exclusion of company users, exposure misclassification and insufficient duration of follow-up [15, 16]. However, regarding acoustic neuroma the mean size of the tumors was significantly larger for cellular phone users than for nonusers

[17]. These results have been discussed regarding limits in design and interpretation of results [18]. A recent Swedish study confirmed an increased risk for acoustic neuroma associated with cellular telephone use [19]. However, the study has been criticized for, e.g. inclusion of cases not reported to the Swedish Cancer Registry, inconsistent numbers in tables and inappropriate analysis of data [20]. A comparison of latency periods and cumulative number of hours for cellular phone use among cases is presented in table 7. Clearly most of these studies have too few subjects with a long latency period and high exposure to have statistical power to detect an increased risk. Our studies have so far the largest number of cases with long-term use of cellular phones. The results of these studies have been discussed in more detail in other papers and we refer to those publications [9, 10].

It should be noted that in the recently presented REFLEX study radio frequency electromagnetic fields (RF-EMF) produced genotoxic effects in cell systems at SAR levels between 0.3 and 2 W/kg with significant increase in single- and double-strand DNA breaks and micronuclei frequency [21]. Significant findings of chromosomal aberrations were observed in fibroblasts and intracellular increase of free radicals in HL-60 cells. It was concluded that RF-EMF might activate several groups of genes that play a role in cell division, cell proliferation and cell differentiation. Furthermore, it was concluded that we are now aware of pathophysiological mechanisms that could be the basis for the development of chronic diseases, such as cancer, in humans. The current SAR level of 2 W/kg based on thermal effects from RF-EMF is thus inappropriate.

In summary, our study showed an increased risk for acoustic neuroma associated with analogue phone use. This is the third case-control study showing a link between significantly increased risk for acoustic neuroma and cellular telephone use [5, 6, 19]. Regarding meningioma, a somewhat increased risk was found, although the association was not as clear as for acoustic neuroma.

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