Are cell phones safe? - A pilot meta-analysis of case control studies linking cellphone use to acoustic neuroma

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Abstract

This pilot meta-analysis based on few reports has suggested a weak association between cellphone use and the risk of acoustic neuroma. These findings will need confirmation by analysis of more research reports. The results of the expanded study will be used as the basis for planning a long-term prospective study of the risk of cancer among long-term users of cell phones.

Introduction

Acoustic neuroma is a benign, slow growing tumor of the 8th cranial nerve. It presents with otological symptoms (tinnitus, vertigo, and hearing loss) and signs (abnormal hearing tests, facial numbness and weakness, and papilledema). Larger tumors can cause symptoms and signs due to compression of the brain stem and involvement of the facial and trigeminal nerves. Men are affected more than women. Presentation is above 30 years. Elderly patients without serious symptoms and signs are left untreated but are followed up for complications. Micro surgery, radio surgery or a combination of the two may be used in treatment.

Electromagnetic radiation is a known cause of cancer. The localized radio frequency microwave energy emitted by cell phones has been suspected as a cause of brain malignancies. This is an issue of public concern because cell-phone use is increasing very rapidly in Brunei and other countries. Evidence indicates that the incidence of brain tumors has been rising in the recent past when cell-phone use became very popular. Hardell et al found a significant increase of +0.80% in the incidence of all brain tumors taken together for the 1960-1998 [1]. The risk of cancer in association with cell-phone use has also been observed to

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Omar Hasan Kasule Institute of Medicine, Universiti Brunei Darussalam, Jalan Tungku Link, Gadong BE 1410, Brunei Darussalam rise in the same period. Hardell et al 2003 in a computation of annual risk increase by treating exposure as a continuous variable showed increase of risk with time the annual risk increase being 1.04 (1.01 - 1.08) [2].

Evidence of the relation between radio frequency electromagnetic fields and brain tumors has been contradictory. Some authors found no relation while others found the evidence to be weak and unconvincing [3-5]. The studies reviewed below show weak or insignificant association. Considering all brain tumors together, Hardell et al. 2002 in a study of 588 cases and 581 controls found the following odds ratios with 95% confidence intervals for analog cell-phones 1.13 (0.86 - 1.48); for cordless phones 1.13(0.85 - 1.50); and for digital cell-phones OR = 1.59 (1.05) -2.41). Ipsilateral use increased the risk [6]. Hardell et al 2002 in a study of 1617 cases and 1617 controls found the risk for short term exposure to analog telephones to be OR = 1.3 (1.02 - 1.6) and for long term exposure OR = 1.8 (1.1)-2.9). The risk was higher on the same side. There was no significant risk from cordless or digital cell-phones[7]. Hardell at al 2004 reported the overall risk of using analog telephones to be OR = 1.31 (1.04-1.64). The risk increased to OR = 1.65 (1.19 - 2.30) for ipsilateral use. Risk was highest among the 20-29 age group with the ipsilateral risk being OR = 5.91 (0.63 - 55). This age group experienced a raised ipsilateral risk if the latency period was over 5 years with OR = 8.17 (0.94-71) for analog phones[8]. Lonn et al 2004 in a study of 148 cases and 604 controls found the risk of acoustic neuroma from mobile phone use to be OR = 1.0 (0.6 - 1.5) for short term use and OR = 1.9 (0.9 - 4.1)for long term use. The risk was increased on the same side [9]. Hardell et al 2006 in a study of 317 cases and 692 controls found the following risks for various cell-phones and durations of use. The risk for analog cell-phones was OR = 2.6 (1.5-4.3) for short term use and OR = 3.5 (2.0 - 6.4) for long term use. The respective risks for digital cell phones were OR=1.9 (1.3-2.7 and OR=3.6 (1.7-7.5) and for cord-less phones OR=2.1 (1.4-3.0) and OR=2.9 (1.6-5.2). Multivariate analysis showed all three phone types to be associated with increased risk[10].

This article reviews case control studies relating cell-phone use to acoustic neuroma. Hardell et al 2003 in a study of 1429 cases and 1470 controls found the risk of acoustic neuroma among analog telephone users to be OR = 4.4(2.1-9.2)[2]. Hardell et al 2005 in a case control study of 84 acoustic neuroma cases found the risk from analog phones to be OR = 4.2 (1.8 - 10) for the short term and OR = 8.4 (1.6-45) for long term exposure. The risk for digital phones was OR = 2.0 (1.05 - 3.8). Cordless phones did not show increased risk. Multivariate analysis showed analog phones to be an independent risk factor for acoustic neuroma [11]. Schoemaker et al 2005 in a study of 678 cases and 3553 controls found no increased risk of acoustic neuroma from regular cell-phone use. This applied even if the analysis was carried out separately for analog and digital cell-phones. Risk was increased for the same side and for long term exposure OR 1.8 (1.1 - 3.1) [12]. Takebayashi et al 2006 in a study of 101 cases and 339 matched controls found no association between cell-phone use and acoustic neuroma. There was no association between risk and cumulative years of cell-phone use[13]. Hardell et al 2006 in an analysis of 2 pooled case control studies with 1254 cases and 2162 controls found the risk of acoustic neuroma to be OR = 2.9 (2.0 - 4.3) for analog cell-phones, OR = 1.5 (1.1)-2.1) for digital cellphones, and OR = 3.8 (1.4 - 10) for cordless phones. The risk for analog cell-phones increased if exposure was >15 years to OR = 3.8 (1.4 - 10). Multivariate analysis showed use of analog cell-phones to be an independent risk factor for acoustic neuroma[14]. Schlehofer et al 2007 in a study of 97 cases and 194 matched controls found the risk of acoustic neuroma from regular mobile phone use to be OR = 0.67 (0.38-1.19)[15].

We can conclude from the literature survey above that studies relating cell-phone use and brain cancers in general are either negative or show a weak association but the trend to increasing risk with longer duration of cell-phone use is very clear. This indicates that the risk may exist but is not detected due to 3 methodological defects explain the results: duration of follow up not sufficient, inaccurate measurement of the level of exposure and biases of response and recall [16].

The present study is a review of recent studies on cell phone use and acoustic neuroma. The objective of this preliminary study is to derive an estimate of acoustic neuroma risk by combining data from a few case control epidemiological studies. This is a pilot study that will be extended to include more studies as soon facilities for extensive literature search are available. All these efforts will culminate in the design and execution of a long-term prospective study in Brunei of the relation between cell-phone use and risk of various malignancies. Brunei has an advantage for such a study because of ease of follow up in a small population.

Methods

Five case control studies from the Interphone international collaborative study of the association between cell-phone use and cancer were identified with the help of PUBMED. The studies were all carried out using the same protocol so they had similar design and analytic methods. Tables 1 and 2 summarize the salient features of each research report. The odds ratio with 95% confidence intervals was abstracted from each report. Other essential data abstracted were: type of cell phone used, years of cellphone use <10=short, >10= long), and number of study subjects. The inverse variance meta analytic method was used compute a pooled odds ratio over several studies by summation of the odds ratios of individual studies each being weighted by the inverse of its variance. $OR_n = \sum w_i OR_i \sum w_i$ where OR_p = pooled odds ratio, w_i = weighting which is the inverse of the variance of the odds ratio. The 95% Confidence Intervals were computed using the standard error $S(OR_p) = 1/sqrt{\Sigma w_i}$. Heterogeneity was tested using $\chi = \sum w_i (OR_i - OR_p)^2$ where $w_i = 1/S_i^2$. All computations were carried out using log-transformed data.

Author and type of phone	Country anddates	Study subjects	OR (95% CI)
Takebayashi et al. 2006	Japan	101 cases;	Short term OR = 0.73 (0.43, 1.23)
	2000-2004	339 controls	Long term OR = 1.09 (0.58, 2.06)
Schoemaker MJ, et al. 2005	UK. Sweden, Norway, Denmark.	678 cases	Short term $OB = 0.9 (0.7, 1.0)$
	Funland	3553 controls	Long term $OR = 1.8 (1.1-3.1)$
Lonn et al. 2004	Sweden	148 cases	Short term OR = 1.0 (0.6,1.5)
	1999-2002	604 controls	Long term OR = 1.9 (0.9 – 4.1)
Schlehofer et al. 2007	Germany.	97 cases	Short term OR = 0.67 (0.38, 1.19)
		194 controls	

TABLE 1: STUDIES WITH NO MENTION OF THE TYPE OF PHONE

TABLE 2: STUDIES THAT GAVE SEPARATE DATA FOR ANALOG AND DIGITAL CELLPHONES

Author	Country	Study subjects	Odds Ratio (95% CI)
Hardell L et al 2005.	Sweden	84 cases 692 controls	Short term analog OR = 4.2 (1.8,10) Long term analog OR = 8.4 (1.6,45) Short term digital OR = 2.0 (1.05,3.8)
Hardell L, et al. 2006	Sweden	1254 Cases 2162 controls.	Short term analog OR = 2.9 (2.0, 4.3) Long term analog OR = 3.8 (1.4, 10) Short term digital OR = 1.5 (1.1, 2.1)

Results

Tests for heterogeneity were negative so pooled effect measures were computed. There was no strong, consistent, and significant association between cell phone use and acoustic neuroma in the short term (less than 10 years of use). The data did however suggest increasing risk with long-term use, use of analog cell phones as compared to digital phones, and disease on the same side of the head as the cell phone is usually held. For research reports without specification of the type of cell-phone, the pooled effect estimates (95% confidence limits) were $OR_p = 0.9$ (0.7, 1.0) for short term use and $OR_p = 1.6$ (1.1, 2.2) for long term cell-phone use. The pooled effect measures for analog cell-phones were $OR_p = 3.1$ (2.2, 4.4) for short term use and $OR_{p} = 4.3$ (2.2, 8.1) for long term use. The pooled effect measure for digital cell-phone use in the short term was 1.6 (0.51, 4.9). Data was not available for long term digital cell-phone use.

Discussion

The data suggests association between use of analog cellphones with acoustic neuroma. The association is significant for analog cell-phone short term follow up. It is stronger for long term analog cell-phones on longer term follow up but does not reach significance due to the large variance based on few research reports. Analysis of more research reports is needed to confirm these findings.

The data quality was high being collected under a uniform INTERPHONE protocol. The studies were also similar in design and data collection because they largely used the same protocol. Lack of detailed raw data prevented use of the Mantel-Haenszel method and sparsity of the data prevented control for confounding. Use of self-reported questionnaires had limitations in accurate measurement of the total duration of use, frequency of use every day, position in which the cell phone is used, type and power of the phone used. More accurate exposure information can be obtained from the billing records of cell phone subscriber companies which have detailed automated data on times of calls, duration of the calls, type of phone and strength of the radiation energy emitted. It is however doubtful that these companies will cooperate because of business self-interest. A study in Denmark found that there was a fair agreement between self-reported cell-phone use and subscriber data. Risk measures based on the two exposure measurements were not very different from one another. Each of the 2 methods has its limitations[17]. The fair agreement between the 2 methods is good news because we can rely on self-reported use that we can get easily instead of trying to obtain subscriber information that is not easily accessible. Exposure assessment is the weak link in studies of the association between cell-phone use and cancer. Self reported use of cell-phones is unreliable for duration of exposure. The relationship between duration of use and strength of the electromagnetic field is not known. In view of these limitations prospective studies will be needed to settle the questions under study [18].

The current analysis has not showed a strong, consistent, or conclusive evidence of a link between cell phone use and acoustic neuroma although the data suggests such a link. Definitive answers will be obtained from studies of longer-term prospective studies because cancer has a long induction period.

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