RESEARCH ARTICLE

Lack of Sunlight Exposure Influence on Primary Glioblastoma Survival

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Abstract

Background: The prognosis of primary glioblastoma (GBM) is poor. Approximately 2/3 of primary brain tumor diagnoses are GBM, of which 95% are primary lesions. In this study, we aimed to evaluate whether more sunlight exposure has an effect on survival of patients with primary GBM. Materials and Methods: A total of 111 patients with primary GBM were enrolled from Kayseri in inner Anatolia which has a cold climate (n: 40) and Mersin in Mediterranean region with a warm climate and more sunlight exposure (n: 71). The patients with primary GBM were divided into two groups as Kayseri and Mersin and compared for progression free survival (PFS) and overall survival (OS). Results: The PFS values were 7.0 and 4.7 months for Kayseri and Mersin groups, respectively (p=0.10) and the repsective OS values were 13.3 and 9.4 months (p=0.13). We did not found any significant difference regarding age, sex, comorbidity, smoking, surgery, resurgery, adjuvant chemoradiotherapy and palliative chemotherapy between the groups. Conclusions: We found that more sunlight exposure had no impact on prognosis of patients with primary GBM, adding inconsistency to the literature about the relationship between sunlight and GBM.

Keywords: Glioblastoma - sunlight - vitamin D - survival - brain tumor

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Introduction

Glioblastoma (GBM) is the most common type of primary brain tumor and it represents 2/3 of primary brain tumor diagnosis (Muallaoglu et al., 2014). GBM is highly invasive, generally incurable and rapidly fatal (Zeybek et al., 2013) . Its prognosis is poor and its 2-year-overall survival (OS) and 4-year-OS are 26% and 12%, respectively (Stupp et al., 2005) and median survival time is between 5.7- 15.2 months in different studies, approximately (Hyun et al., 2013). The median age at the time of diagnosis is 64 and 45 years for glioblastomas and anaplastic gliomas, respectively (Bhurgri et al., 2011; Ahmed et al., 2014). Although GBMs are similar morphologically, they are categorized according to clinical presentation: Primary and secondary GBMs. Primary GBMs develops de novo from glial cells and accounts for 90% of patients with GBM (Furnari et al., 2007). Primary GBMs have clinical history of 6 months and generally occur in older patients (Reardon and Wen, 2006). Secondary GBMs develops from low grade gliomas and anaplastic astrocytoma (Parsons et al., 2008).

Some studies reported that radiation, tobacco, alcohol, head trauma, exposure of N-nitroso compounds were risk factors (Giles et al., 1994; Inskip et al., 1998; Braganza et al., 2012). Additionally, some studies found an increased incidence of brain cancer among white collar professionals, electrical, oil refinery and agriculture workers (Savitz and Loomis, 1995; Musicco et al., 1988; Preston-Martin, 1998). It was reported an inverse relationship between history of allergies, fruit and/or vegetables intake and brain tumors (Chen et al., 2002; Schwartzbaum et al., 2012).

Because of incidence of cancer is different among geographic areas, sunlight exposure has been investigating in etiology of cancer. Turkey consists of different geographic areas according to sunlight exposure. The Mediterranean region has a warmer climate, whereas internal regions are colder, especially during winter. Annual solar light exposure is more intensive in the Mediterranean region than internal regions.

In present study, we evaluated whether more sunlight exposure had an effect on survival in patients with primary GBM and we compared the patients with primary GBM from different region those have different sunlight exposure in state of disease free survival (DFS) and overall survival (OS).

Materials and Methods

Totally of 111 patients with GBM enrolled from Kayseri (n: 40) and Mersin (n: 71). Kayseri state locates in inner Anatolia which has a colder climate. Mersin state locates

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in Mediterranean region with a warmer climate. Mersin region has more sunlight exposure than Kayseri region. The patient informations were recorded from Acibadem Kayseri Hospital and Kayseri Training and Research Hospital in Kayseri and from Mersin Government Hospital in Mersin. All patients had grade IV GBM and the characteristic of their disease is primary GBM. The patients were divided into two groups as Kayseri and Mersin regions. The hours of sunny days according to region, age, sex, comorbidity, smoking, surgery types, adjuvant chemoradiotherapy, secondline chemotherapy, the date of diagnosis, the time of progression, the date of death of patients with GBM were recorded to Statistical Package for the Social Sciences 16.0 (SPSS 16.0, SPSS Inc., Chicago, IL, USA) statistical programme.

Statistical analysis was performed using the SPSS software version 16.0. According to regions sunny days were compared using two independent samples t test. To determine properties of patients with GBM, mean, frequencies analysis, two independent samples t test and chi-square tests were performed. The effect of sunlight exposure on PFS and OS of patients with GBM was investigated using log-rank test. The Kaplan-Meier survival estimates were calculated. p value <0.05 was considered significant.

Results

The hours of sunny days of Kayseri and Mersin regions were depicted in Table 1 and shown in Figure 1. Except for June, July and August, the hours of sunny days were higher in Mersin than Kayseri. Annual total hours of sunny days were 2494.9 and 2747.3 hours for Kayseri and Mersin region, respectively (p=0.56). The mean age of Kayseri and Mersin groups were 54.5±14.2 and 56.8±13.1 years, respectively (p=0.41). It was no found any significant difference regarding age, sex, comorbidity, smoking, primary surgery, resurgery, adjuvant chemoradiotherapy and secondline chemotherapy between groups (p=0.41, p=0.49, p=0.24, p=0.15, p=0.38, p=0.25, p=0.59 p=0.13, respectively). These results were depicted in Table 2.

The PFS values were 6,96 and 4,73 months for Kayseri and Mersin groups, respectively and there was no significant difference (p=0.10). The OS values were 13.3 and 9.4 months for Kayseri and Mersin groups, respectively and it was not found any significant difference between groups for OS (p=0.13). The PFS and OS values were given in Table 3. The PFS and OS curves were shown in Figure 2 and Figure 3.

Table 1. Hours of Sunshine Per Day for Kayseri and Mersin (p=0.56)

Months	Kayseri region Hours of sunshine per day	Mersin region Hours of sunshine per day
January	3	5.6
February	4.6	5.4
March	4.6	6.5
April	6.1	7.3
May	8.2	8.5
June	10.2	10.1
July	11.6	10.1
August	11.2	10
September	9.1	9.2
October	6.4	7.4
November	4.4	5.6
December	2.5	4.5
Total hours (year)	2494.9	2747.3

Table 2. Properties of Groups

Parameters		Kayseri region (n: 40)	Mersin region (n: 71)	p value
Age (mean)		55±14	57±13	0.41
Sex	Male	29 (73%)	47 (66%)	0.49
	Female	11 (28%)	24 (34%)	
Comorbidity	Yes	7 (17.5%)	18 (25.4%)	0.24
	No	33 (82.5%)	53 (74.6%)	
Smoking	Yes	7 (17.5%)	20 (28.2%)	0.15
	No	33 (82.5%)	51 (71.8%)	
Surgery	Biopsy	9 (22.5%)	9 (12.6%)	0.38
	Subtotal	30 (75%)	59 (83.1%)	
	Total	1 (2.5%)	3 (4.2%)	
Resurgery	Yes	3 (7.5%)	2 (2.8%)	0.25
	No	37 (92.5%)	69 (97.2%)	
Adjuvant CRT	Yes	36 (90%)	63 (88.8%)	0.59
	No	4 (10%)	8 (11.2%)	
Secondline CT	Yes	7 (17.5%)	6 (8.5%)	0.13
	No	33 (82.5%)	65 (91.5%)	

Table 3. PFS and OS Values According to Regions

Parameter	Kayseri region	Mersin region	p value
PFS (median-months)	6.96 (5.92-8.00)	4.73 (3.10-6.35)	0.10
OS (median-months)	13.27 (10.39-16.15)	9.43 (7.59-11.26)	0.13

*PFS:Progression free survival; OS: Overall survival

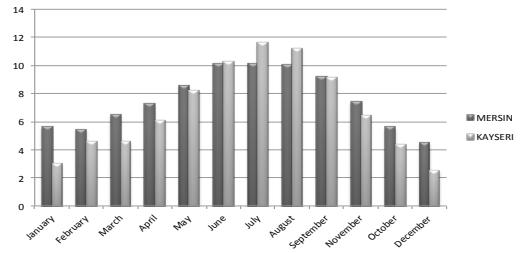

Figure 1. Hours of Sunshine Per Day for Mersin and Kayseri

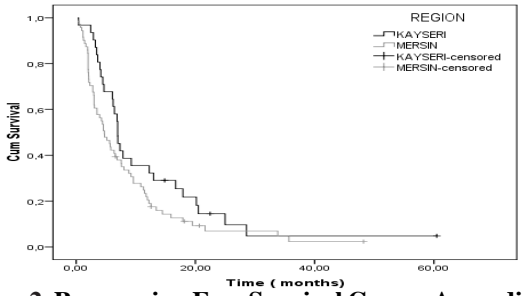

Figure 2. Progression Free Survical Curves According to Groups

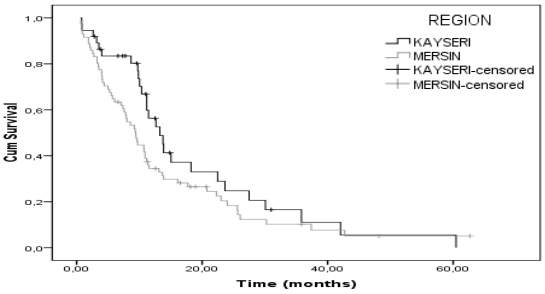

Figure 3. Overall Survival Curves According to Groups

Discussion

In our study, we found that more sunlight exposure had no an effect on prognosis of patients of primary GBM.

There are several hypotheses in explanation of the relationship between season and GBM. One of them is the impact of season on allergies/immunity, farming, vitamin D, diet, viruses those mentioned introduction as risk factor for GBM (Efird, 2010). In addition it was shown that vitamin D transformed to active metabolites via sunlight in the skin can induce cell death in animal and human glioblastoma cell lines (Hakko et al., 2009).

Currently, the literature informations about the relationship between sunlight exposure and GBM are still inconsistent. In a study, it was reported that winter birth is related to risk of brain tumor among Finnish patients with brain tumors (Mainio et al., 2006). Similarly, it was found the association between birth in January-February and risk of GBM (Brenner et al., 2004). Also Hakko et al. reported the mortality rate was more among patients with brain tumor operated on February-March (Hakko et al., 2009). In these studies, the sunlight exposure was less in winter than others. In a review, Grant has reported weaker evidence between ultraviolet B – vitamin D and brain tumor from ecological studies (Grant, 2012). Unlike these studies mentioned above, Yang et al. (2011) had found no association between sun exposure, solarium use, or vitamin D intake, and brain cancer risk.

When evaluated in vitro studies planned to explain the relationship between vitamin D and GBM, generally their results shown vitamin D and its metabolites induce death of GBM cell lines (Naveilhan et al., 1994; Baudet et al., 1996; Magrassi et al., 1998). One of the effects of sunlight exposure on cancer prognosis may be mediated by vitamin D and its metabolites.

Although some studies have reported an inverse relationship between prognosis and risk of GBM and sunlight exposure, in our study, we did not found any relationship between sunlight exposure and prognosis of primary GBM. Both of groups in presented study had similar as socioeconomic, cultural and dietary habits. Dietary intake of vitamin D was similar for both of groups and one of the most important factors those affect the blood level of vitamin D is sunlight exposure. Despite of the difference of sunlight exposure, this difference did not affect the survival of patients with primary GBM.

We may mention some limitations about our study. There are 3 types of ultra-violet (UV) rays: UVC, UVB and UVC. UVC rays are stopped by the earth's atmosphere and they do not reach to the surface of earth. UVB light is the only wavelength that promotes vitamin D production while UVA rays do not promote vitamin D production. UV Index is an international standard measurement of UV (ultra-violet) radiation from the sun for a particular place and time and the measurement of UV Index takes into account UVA and UVB rays. In addition, to live above latitudes (especially >35 degrees) may cause less effective sunlight that is needed for vitamin d synthesis. If the all factors such as UV Index and the degrees of latitude are evaluated together, our study can give the optimal results. This condition may be most important limitation for presented study.

In epidemiologic studies, the incidence of GBM was reported as different than each other (Ding and Wang, 2011; Manoharan et al., 2012). The geographical difference may be related to multiple factors but the relationship between sunlight exposure and primary GBM is still debated. Further studies are needed to clarify the relationship between more sunlight exposure and primary GBM.

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