COMPARATIVE PROSPECTIVE STUDY OF TEMOZOLOMIDE AS A RADIOSENSITIZER BY DIFFERENT PROTOCOLS IN GLIOBLASTOMA MULTIFORM

THESIS

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ABSTRACT

Glioblastoma multiforme is one of the most aggressive brain tumors , which should be maximally resescted as much as possible to obtain further and better outcome . The standard adjuvant treatment at present is radiation therapy concomitant with temodal which approved in multiple phase III trials which demonstrated significant improvement in the outcome and survival of patients .

Keywords

Glioblastoma
Multiforme Radiation
Therapy Temodal

INTRODUCTION

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High-grade gliomas (HGG) is a diverse group of brain malignancies. Glioblastoma (GBM, WHO grade IV) is the most common of these gliomas and it accounts for more than half of all HGGs. Surgery is the initial treatment for patients with a grade III or IV glioma. In addition to providing material for a definitive tissue diagnosis, surgery alleviates symptomatic mass effect and can result in a reduced need for corticosteroids. Advances in surgical techniques and postoperative care have improved surgical outcomes and increased the ability to perform more complete resections safely, which for HGG associates with improved overall survival ***(Stark AM,*** *et al.,* ***2012)***

Postoperative external beam radiation is standard for HGG and as such, efforts have been made to improve efficacy Highly conformal stereotactic radio-surgery and Proton therapy had been evaluated in several large studies none showed additional benefit over standard radiation ***(Souhami L,*** *et al.,* ***2004)***

The current post-surgical standard of care for newly diagnosed GBM is based on the results of a randomized phase III study. It demonstrated that focal radiation with daily concurrent temozolomide and post-radiation TMZ for 5 days every 28 days for up to 6 cycles resulted in a significant increase in overall survival (***Stupp R,*** *et al.,* ***2005)***

Despite modest improvement in the overall survival of patients with GBM in the recent decade, the outcome remains poor. Therefore, the need for more effective novel treatments in this neoplasm is urgently needed.

AIM OF THE WORK

AIM OF WORK

The purpose of the study is to evaluate the efficacy and toxicity of Temozolomide as a radiosensitizer when given daily during radiotherapy versus the administration in first and last weeks of radiotherapy in the term of response rate, overall survival and progression free survival .

REVIEW OF LITERATURE

EPIDEMIOLOGY

Glioblastoma multiforme is the most frequent primary brain tumor, accounting for approximately 12-15% of all intracranial neoplasms and 50-60% of all astrocytic tumors. In most European and North American countries, incidence is approximately 2-3 new cases per 100, 000 people per year (***Fisher JL** et al., **2007).***

The age distribution of brain tumours is bimodal, with a peak incidence in children and a second larger peak in adults aged 45-70 years (***Lantos PL** et al., **2002)***

In Egypt, there is no clear data about the incidence of high grade gliomas in the population. At Al Kasr Al Aini hospital, the incidence of GBM in adult during the period from 2009 till 2012 was 2% among solid tunors and 31.1% among all patients with other brain tumors as in (**Fig. 1)** ***(NEMROCK registration)***

In NCI of Egypt, this group constituted only 0.21% of total malignancy with a slight adult predominance of 54.44% and no sex predilection (50% each). The low number of such tumors could be attributed to the lack of neurosurgery practice at NCI (***Mokhtar N.** et al., **2007)***

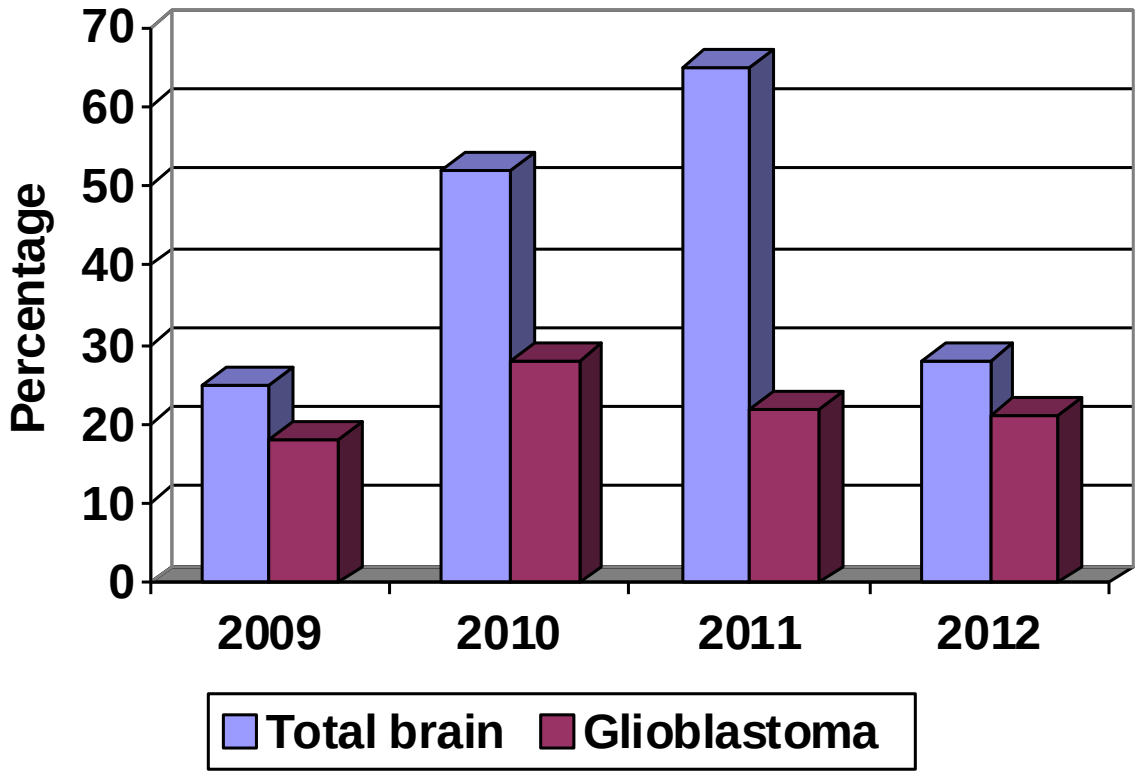

Fig (1): Graph demonstrating incidence of GBM in relation to total brain cases in NEMROCK

RISK FACTORS:

The specific cause of GBM is unknown. Many factors that increase the risk of developing GBM have been suggested:

- The only risk factor that has been proven to increase the risk of developing GBM is exposure to ionizing radiation. Because radiation acts to damage DNA and causes cell death, some side effects of radiation include necrosis of tissue and development of tumors Since the 1960s, over 116 cases of GBM caused by radiation have been reported and it is estimated that overall risk of developing GBM following radiotherapy is approximately 2.5 percent ***(Salvati, 2003).***

- Increased cell phone use has been suggested as possible risk factors for GBM. Cell phones are known to release a small amount of non-ionizing electromagmetic radiation ***(Adamson, 2009).***

- In May 2011 the International Agency for Research on Cancer (IARC) at WHO categorized the radiofrequency electromagnetic fields (RF-EMF) from mobile phones, and from other devices that emit similar non-ionising electromagnetic fields, as a Group 2B, i.e. a 'possible', human carcinogen ***(IARC, 2011)***
- Glioma risk attributable to inheritance has been estimated at 4% and is most commonly associated with neurofibromatosis, tuberous sclerosis, Turcot's syndrome, and Li-Fraumeni syndrome ***(De Angelis LM, 2001)***