Appraisal of carmustine implants and temozolomide for newly diagnosed high grade glioma

Brain and Spine Foundation

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The Brain and Spine Foundation – working with people affected by brain tumours

The Brain and Spine Foundation aims to improve the quality of life for people with brain and spine conditions and reduce neurological disability by providing a national focus for information and education.

The Brain and Spine Helpline answers over 2,500 calls each year on a wide variety of neurological conditions and on average we receive over 200 enquiries from patients and carers affected by brain tumours. Out of those callers to the Helpline who identified the type and/ or grade of their tumour (approximately 50% of callers in total), 20% were people with a high grade glioma (HGG). Most of the enquiries we receive are from carers including friends and family. Each year, we distribute over 1,000 copies of our booklet 'Brain tumours – a guide for patients and carers'. We also receive calls and emails from families with children diagnosed with a brain tumour. Since March 2004, we have distributed over 500 copies of our information resource for children 'Headstrong - all about brain tumours' to children, families and health professionals.

How many people are affected?

Statistics on the number of children and adults diagnosed with brain tumours vary and it widely accepted that current figures underestimate the incidence. There is a slight peak in incidence in early childhood and the brain is the most common site for solid tumours in childhood. Incidence also peaks between the ages of 70-74 yrs.

Whilst the overall rates for cancer mortality have reduced, the prognosis for brain tumour remains poor. Burnet et al. (2005) calculated that Brain and CNS cancers result in just over 20 average years of life lost, the highest for all cancers. In adults, even with treatment (surgery, radiotherapy and chemotherapy), the median survival time is about one year (Beers and Berkow, 1999)

Living with a high grade glioma

Brain tumours cause a wide range of symptoms as a result of the general effects of raised intracranial pressure and also focal neurological deficits. These include headaches, nausea, visual disturbance, speech and language problems, cognitive and behavioural changes and motor deficits. In contrast to many other cancers and life-limiting conditions, the cognitive effects and changes in personality can occur at onset. Mobility and communication are frequently impaired and consequently quality of life is severely compromised. Furthermore, the side effects of treatment can be severe and disabling.

Consulting with patients and families affected by brain tumours

The Brain and Spine Foundation, in collaboration with the United Brain Tumour Campaign, conducted a survey of people affected by brain tumours, primarily to ask about their experiences of neurological services. 102 patients and carers affected by brain tumours completed the survey. 14% of the respondents were from carers of children with a brain tumour. Respondents had a wide range of tumour types but 19% had been diagnosed with an astroyctoma and 10% with a glioblastoma multiforme. Nearly half of all respondents wanted information on treatment options and over 40% would have liked information on clinical trials. These results highlight the desire of patients affected by brain tumours to explore different treatment options. This is supported by an audit of calls to the Brain and Spine Helpline which showed that nearly all of the calls received from patients and carers with HGG were seeking information on clinical trials or alternative treatments after more 'conventional' therapeutic options had been exhausted.

As part of the preparation for our submission, we contacted a small group of people affected by HGG who had experience of the technologies being considered in this appraisal. Telephone interviews were conducted with five people who were currently looking after, or had looked after, a family member with a HGG.

The effectiveness of temozolomide (TMZ)

Current treatment options for high grade gliomas include surgery, radiotherapy and chemotherapy. In March 2005 the FDA approved the use of TMZ for adults patients with GBM when administered in combination with radiotherapy and then as a maintenance therapy.

Research studies suggest that adults with HGG who receive TMZ have increased survival times and experience relatively few side effects (e.g, Stupp et al., 2005). There is also emerging evidence to support the use of TMZ in the paediatric population (e.g., Verschuur et al., 2004).

Whilst patients and carers interviewed recognised that TMZ is not a 'cure' for HGGs they were very keen to emphasise the positive impact this treatment had on quality of life and life expectancy. This is particularly important for patients with HGGs who may only survive for a few months after diagnosis.

"The temozolomide worked almost immediately. Speech came back, energy levels increased, mobility improved. It changed his life."

Through a significant improvement in symptom control, patients were given valuable extra quality time with their families.

"Everything, apart from the time on the temozolomide was all bad. If we hadn't had the five months together when he was on the temozolomide there would not had been any happy memories at all".

Side effects

"Most people will go for any option they are given, but maybe not if there are really awful side effects. You might start to question your decision and whether you should accept there is nothing you can do. But we have experienced no side effects".

None of the people interviewed could identify any negative effects of TMZ. One carer spoke about how they needed to balance the side effects of treatment against the expected benefits.

"One of the best things about temozolomide is that we haven't had to change our life style…Temozolomide doesn't restrict your life style….you can still have a drink, eat what you want and do what you want. It's these small things that make the difference".

The psychological and financial burden of repeated hospital visits was frequently mentioned as a source of concern and distress in our consultation work with children and adults affected by brain tumours. Transport can be difficult to organise and journey times exhausting and stressful. TMZ can be administered at home and with minimal visits to the hospital thus conferring significant benefits over some other treatment options.

Offering hope

An important theme emerging out of our work with patients with HGG is the need for hope and to be given a treatment option even if it not a cure for their condition.

"There currently is no cure for brain tumours and whilst we all hope that someday there will be, there are people who need help now. When there is no cure, quality of life is what counts and we need to push forward those treatments that can improve this".

"Some people do live 4/5 plus years with a GBM, you obviously want to be one of those people. Some doctors think the jury is out (the trial evidence is not clear) but you need to give someone a chance. Maybe TMZ will give us the chance to be around to try any new treatment that might be around in a few years time".

The use of TMZ in the older patients

Elderly patients may be excluded from current treatment options due to the perceived side effects and risks associated with therapy. For example, radiotherapy and chemotherapy may not be so well tolerated as in younger patients. One patient population for which TMZ may have a significant benefit is in older people. Research studies have demonstrated that TMZ is well tolerated in this patient group and there is evidence that it slows disease progression (Brandes and Monfardini, 2003).

The effectiveness of carmustine implants

The FDA approved the use of carmustine implants for patients with newly diagnosed malignant gliomas as an adjunct to surgery and radiation. Current studies indicate that there is an increased survival time of approximately two-three months.

Side effects of carmustine implants

Side effects include intracranial infections, abnormal wound healing, cerebral oedema (e.g., Weber and Goebel, 2005). However, it is difficult to ascertain any possible increased incidence of infection due to carmustine versus the effects of the craniotomy alone or tumour regrowth.

Only one of the carers interviewed has any knowledge of carmustine implants and who was currently waiting to see if this treatment option was suitable for treating their partner's tumour. From the information they had received, they would have the carmustine implants inserted. They were unaware of any specific side effects or risks of this treatment as distinct from those associated with the debulking of the tumour.

Summary

In conclusion, in the light of the relative dearth of effective treatment for HGG, any new treatment which confers even modest benefits in terms of improved quality of life, symptom control and prolonged survival should be welcomed. In the absence of any treatment which can cure this condition, patients and their families look towards those treatments which offer some hope, balanced against the risks of any such treatment.

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