GUIDELINES ON THE MANAGEMENT OF SEIZURES IN PATIENTS WITH BRAIN TUMOURS (PRIMARY OR SECONDARY). Dr. Yvonne Hart, Dr. Allyson Parry

The diagnosis and management of patients with seizures is complex and usually requires specialist neurological expertise. Where possible, oncologists are encouraged to refer or discuss the patient with a neurologist.

Who to contact for advice

JRH    Dr Yvonne Hart– ext. 31891, Dr Allyson Parry – ext. 31892
Neurology SpR on call – JRH switchboard
Other hospitals    The local consultant neurologist

How do you establish the diagnosis of a seizure?

This is dependent on an experienced review of the history obtained from the patient and any witnesses.

What are the possible causes of a seizure in this patient group?

i) Presence of a space occupying lesion (seizure often focal onset)
ii) Metabolic derangement e.g., Low Na, Ca
iii) Accelerated metabolism of anti-epileptic drug by another medication
iv) Effect of RT
v) Chemotherapy related (usually with encephalopathy)
vi) Vascular – arterial or venous cerebral thrombosis
vii) Non-compliance with pre-existing anti-epileptic medication
viii) Immunosuppressed patient with an opportunistic cerebral infection

Should the patient be started on anti-epileptic medication?

In general, most (but not all) patients start treatment. However, this decision, along with the particular choice of medication, may be complex. It is recommended that this is done in conjunction with a neurologist.

What anti-epileptic drug (AED) should be started?

Drugs favoured by the authors:
Focal onset seizure – carbamazepine, lamotrigine,
Primary generalised seizure – sodium valproate, lamotrigine

N.B. (i) Sodium valproate and phenytoin can be given intravenously, (if the patient cannot swallow safely or is not able to absorb oral medication adequately), at the same dose as the patient’s usual oral dose (Important - see BNF regarding the rate of intravenous administration).

(ii) Phenytoin can be useful when rapid seizure control is required, or if the AED must be given intravenously. However, the use of phenytoin as a long-term AED is not recommended by the authors. Ideally, the patient should be discharged with a plan to switch to an alternative medication, under appropriate supervision.
**Summary of commonly used anti-epileptic drugs**

Each of these four drugs can be used for both partial (focal onset), and generalised (tonic-clonic) seizures. All drugs are potentially teratogenic. This table must be used in conjunction with the BNF, particularly regarding the rate of dose escalation.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Start dose/day</th>
<th>Common maintenance dose/day</th>
<th>Dosage interval</th>
<th>Interactions*</th>
<th>Common Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>200mg</td>
<td>400-1200mg</td>
<td>bd</td>
<td>Enzyme Inducer</td>
<td>Dizziness, diplopia, nausea, rash</td>
</tr>
<tr>
<td>Slow Release</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenytoin</td>
<td>200mg</td>
<td>250-450mg</td>
<td>od</td>
<td>Enzyme Inducer</td>
<td>Rash, gum hypertrophy, hirsutism</td>
</tr>
<tr>
<td>Valproate</td>
<td>600mg</td>
<td>600-2000mg</td>
<td>bd</td>
<td>Enzyme Inhibitor</td>
<td>Weight gain, tremor, hair loss, platelet dysfunction++</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>25mg (except in patients on valproate, when use 25mg alt day)</td>
<td>100-400mg</td>
<td>bd</td>
<td>Probable enzyme inducer</td>
<td>If rash - discontinue, fatigue, headache, dizziness, diplopia</td>
</tr>
</tbody>
</table>

*Enzyme inducers may reduce the plasma concentration of other hepatically metabolised drugs e.g., oral contraceptive pill, corticosteroids. Enzyme inhibitors may increase the concentration of other hepatically metabolised drugs, e.g., valproate increases the plasma concentration of temozolomide and lamotrigine.

++ Sodium valproate can cause platelet dysfunction and/or thrombocytopenia. Platelet function tests should therefore be performed prior to any surgery.

**Is fairly rapid seizure control required (NOT status epilepticus)?**

Patients can be loaded with phenytoin (15mg/kg/24 hours) either orally or iv, before starting a maintenance dose. Valproate therapy can also be initiated quickly (BNF)

**Special note on the non-linear pharmokinetics of phenytoin**

Small increases or decreases in the dose of phenytoin can result in large increases or decreases in the plasma concentration. This can result in either neurotoxicity (nausea, ataxia, dysarthria, mental slowing and nystagmus), or a decline in seizure control, respectively. After a daily dose of 250mg, do not alter the daily dose of phenytoin by more than 50mg/increment. It is recommended that a phenytoin level is then checked a week later before further dose alterations are made.

**Monitoring of drug levels**

With the exception of phenytoin (see above), monitoring of plasma drug levels is not recommended, unless clinically indicated.

**The patient who has been started on AED (usually pre-operatively), with NO history of seizures. When do you stop the AED?**

We recommend that AED are stopped 2 weeks post-operatively. However, it is important that this decision is discussed with the relevant neurosurgeon.