WCN

Symptom management in Neuro-Oncology: anticonvulsants, steroids and anticoagulants

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Learning objectives

- Treating symptomatic epilepsy in brain tumor patients with high efficacy and good tolerability
- Avoiding, recognizing and treating side effects of corticosteroids in brain tumor patients
- Understanding risk benefit ratios of anticoagulation in brain tumor patients

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Symptomatic epilepsy in brain tumor patients

- High incidence
- High risk of cognitive side effects of pharmacotherapy
- High risk of relevant interactions of pharmacotherapy
- Controversies regarding duration of treatment and choice of agent

Incidence of symptomatic seizures

• Low-grade gliomas	70% (manifestation)
• Glioblastomas	35% (manifestation) 30% (disease course)
• Oligodendrogliomas	70-90% (manifestation)
• Metastases	15-25%
• Meningiomas	20-70%
• ZNS lymphomas	15%

Anticonvulsive therapy in brain tumor patients

- **Primary prophylaxis: treat all brain tumor patients?**
- **Primary prophylaxis: prior to surgery in all patients?**
- **Secondary prophylaxis: treat after the first seizure?**
- **Secondary prophylaxis: which agent?**
- **Secondary prophylaxis: what if no success?**
- **Secondary prophylaxis: how long if successful?**

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  Multiple choices, but not all are good…..
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Anticonvulsive therapy in brain tumor patients

Old school drugs & Side effects

Phenobarbitone	**Sedation, allergy** **Enzyme induction (cytochrome P450)**
Phenytoin	**Dizziness, allergy, liver enzymes↑, gingival hyperplasia, cerebellar atrophy** **Enzyme induction (cytochrome P450)** **Increased dexamethasone requirement (50%)**
Carbamazepine	**Dizziness, nausea, ataxia, hyponatremia, gaze-evoked nystagmus, saccadic eye movements, allergy, liver enzymes↑** **Enzyme induction (cytochrome P450)**
Valproic acid	**Tremor, weight gain, coagulation disorders, thrombopenia, teratogenicity** **Enzyme inhibition: increased toxicity of cytotoxic agents**

Anticonvulsive therapy in brain tumor patients

New(er) drugs & Side effects

Lamotrigine	**Allergy, tremor, sedation (rare)**
Gabapentin	**Sedation**
Levetiracetam	**Sedation (rare), psychiatric side effects**
Topiramate	**Sedation, fatigue, inappentence, psychosis**
Lacosamide	**Dizziness, fatigue**

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Anticonvulsive therapy in brain tumor patients

Interactions with chemotherapy

- **Enzyme-inducing anticonvulsants (phenobarbitone, phenytoin, carbamazepine) may reduce the efficacy of cytotoxic agents (vincristin, epipodophyllotoxins, taxanes, alkylators, methotrexate) and steroids**

- **Cytotoxic agents (cisplatin) may reduce the activity of anticonvulsants (phenytoin, valproic acid, carbamazepine)**

- **Enzyme-inhibitory anticonvulsants (valproic acid) may increase the toxicity of cytotoxic agents**

- **Probably no interactions for lamotrigine, gabapentin, levetiracetam, topiramate or lacosamide**

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  Combination or alternative monotherapy
- **Secondary prophylaxis: how long if successful?**

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  Depending on histology, prognosis, tolerability…

Anticonvulsive therapy in brain tumor patients how long if successful?

- **Only preoperative seizures: try to taper within three months of surgery**
- **Postoperative (> 48-72 h) seizures: commonly treatment for life**
- **Surgery-independent freedom from seizures for one year and favorable tumor prognosis: try to taper (again)**
- **Surgery-independent freedom from seizures for one year and unfavorable tumor prognosis: individual decision, consider tolerability versus consequences of seizures, e.g., fractures with bone metastases or osteoporosis**

Overview

Anticonvulsive therapy in brain tumor patients

Agent	Trade name	Dose (mg)	Serum level (µg/ml)	Cost/day (CHF)
Phenobarbitone	zB Luminal®	50-300	10-40	0.1-0.5
Phenytoin	zB Phenhydan®	200-350	10-20	0.15-0.5
Carbamazepine	zBTegretol®	600-2000	4-8	0.7-2.5
Valproic acid	zB Orfiril®	1200-2400	50-100	1-2
Lamotrigine	zB Lamictal®	100-300	2-15	3-7
Gabapentin	zB Neurontin®	900-2400	2 - 20	2-5
Topiramate	zB Topamax®	50-200	2 - 25	2-5
Levetiracetam	Keppra®	1000-3000	5 - 30	4-13
Lacosamide	Vimpat®	100-400	5 – 10	4-13
Zonisamide	Zonegran®	300-500	10 - 40	5-12

Key message I
Anticonvulsants

- Efficient control of symptomatic epilepsy is often possible in brain tumor patients
- It greatly impacts quality of life of patients and carers
- Increasing complexity of cancer pharmacotherapy and repertoire of anticonvulsants requires expertise and specialization

Steroids in Neuro-Oncology

- **Tumor-associated vasogenic edema responds well to corticosteroids**
- **Edema is a major cause of neurological morbidity**
- **Prolonged corticosteroid use has a major negative impact on quality of life**

Adverse events and side effects of corticosteroids

- Cushing syndrome
- Immunosuppression
- Myopathy
- Osteoporosis
- Vascular complications
- Depression, psychosis, cognitive decline

Key message II
Steroids

- **Golden rule for steroid use in Neuro-Oncology: *as much as necessary, as little as possible***
- **No use of corticosteroids in patients with suspected primary CNS lymphoma**
- **Regular monitoring of corticosteroid-associated side effects and adverse effects**

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Vascular complications in Neuro-Oncology

- **Deep vein thrombosis**
- **Pulmonary embolism**
- **Arterio-arterial embolism: surgery-associated, radiogenic, tumorigenic**
- **Increased risk with cytotoxic and anti-angogenic therapies**

Key message III
Anticoagulants

- Deep vein thrombosis and pulmonary embolism are probably underdiagnosed and undertreated in brain tumor patients
- Experience with novel anticoagulants is limited
- Drug drug interactions gain increasing importance

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