Treatment of Myoclonus

The treatment of myoclonus depends on the underlying disorder.

Reversible causes of myoclonus include some toxic–metabolic states, drug intoxications or surgically treatable lesions, however in the majority of cases, the underlying cause is not correctable and symptomatic treatment is the only possibility.

A useful approach to the treatment is to first establish the physiology of myoclonus (cortical versus subcortical or spinal), because different drugs will work in different types of myoclonus.

One single agent can seldom completely control myoclonus; therefore multiple drug trials and combination of drugs are necessary, often in large dosages.

In general, antiepileptic drugs such as valproate, levetiracetam and piracetam are effective in cortical myoclonus, but ineffective in other forms of myoclonus. Clonazepam may be helpful in all types of myoclonus.

Cortical Myoclonus

Treatment of cortical myoclonus is aimed at enhancing deficient GABAergic inhibitory neurotransmission. As a rule, cortical myoclonus is treated with a combination of drugs. Sedation and ataxia are the main side effects of polytherapy, but they may be overcome with the 'start low, go slow' principle. Of the GABAergic drugs, sodium valproate is the most effective. It should be introduced slowly and titrated up to 1200–2000 mg daily. Benzodiazepines are also very useful, especially clonazepam in large doses (up to 15 mg a day). Tolerance may develop after several months, while rapid reduction or withdrawal can produce marked deterioration. Piracetam and levetiracetam are two related drugs, proven to be very useful in myoclonus, although their exact mechanism of action is poorly understood. Large doses of piracetam may be required (3200–4800 mg tds, maximum up to 20 g/day), but levetiracetam is a more potent drug (maximum 3000 mg daily).

In cortical myoclonus, piracetam or levetiracetam can be combined with sodium valproate and clonazepam. Primidone and phenobarbital are rarely effective, whereas zonisamide has helped in some cases of PME.

Phenytoin, carbamazepine, lamotrigine and vigabatrin are best avoided in cortical myoclonus, as they may paradoxically exacerbate myoclonus. This is particularly the case with phenytoin in Unverricht–Lundborg disease. Treatment of PME is very challenging, as drugs that help generalized seizures may worsen myoclonus and vice versa.

Negative Myoclonus

ENM in children suffering from idiopathic partial epilepsy may respond to ethosuximide and levetiracetam. ENM associated with symptomatic or cryptogenic epilepsies is usually less
responsive to common antiepileptic drugs and may be worsened by carbamazepine, valproic acid, phenytoin, lamotrigine and oxcarbazepine. In posthypoxic myoclonus, distal action and reflex myoclonus of upper limbs respond to therapy much better than NM of proximal lower limbs, which causes gait disturbances and frequent falls.

**Subcortical Myoclonus**

Antiepileptic drugs used in cortical myoclonus are not effective in subcortical myoclonus. Clonazepam is useful in hyperekplexia and partially in reticular reflex myoclonus. Myoclonus dystonia responds partially to clonazepam, although the response fails to match that from alcohol. In one report, alcohol-sensitive myoclonus dystonia was successfully treated with 6.125 g/day of gammahydroxybutyric acid. Severe cases of myoclonic dystonia can be helped by bilateral pallidal or thalamic deep brain stimulation.

**Spinal Myoclonus**

In spinal myoclonus, pharmacological treatment is unsatisfactory. Clonazepam is the drug of first choice for both types of spinal myoclonus and dosages up to 6 mg are needed to diminish spinal segmental myoclonus. Levetiracetam was reported to be effective in a series of three patients with spinal segmental myoclonus.

**Segmental Myoclonus**

Segmental myoclonus, irrespective of its origin (palatal tremor, spinal segmental myoclonus) may be treated with botulinum toxin injections, with variable success.

**Peripheral Myoclonus**

In peripheral myoclonus, drugs are usually ineffective, although carbamazepine may have some effect. Hemifacial spasm responds excellently to botulinum toxin injections.

**Psychogenic Myoclonus**

Psychogenic myoclonus may improve as a result of placebo or psychotherapy.