Myoclonus
A Practical Guide to Drug Therapy

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Summary

Several different types of myoclonus can be distinguished on physiological grounds. Cortical myoclonus arises from an abnormal discharge in the somatosensory motor cortex and corticospinal pathways. Brainstem reticular reflex myoclonus and hyperekplexia are forms of generalised myoclonus arising in the brainstem, and palatal myoclonus is a segmental form of brainstem myoclonus. Ballistic overflow myoclonus occurs in hereditary essential myoclonus. Propriospinal myoclonus consists of axial jerks of spinal origin, while segmental spinal myoclonus is thought to arise as a result of the isolation of spinal motoneurons from inhibitory influences or from direct cellular injury.

Treatments of first choice for cortical myoclonus are valproic acid (sodium valproate) and clonazepam. Primidone and phenobarbital (phenobarbitone) may also be useful. However, most patients require polypharmacy for adequate symptomatic improvement. Piracetam has advantages in these circumstances, as its addition to existing treatments is rarely accompanied by sedation. 5-Hydroxytryptophan in combination with carbidopa is now rarely used because of gastrointestinal adverse effects.

In patients with brainstem reticular reflex myoclonus, valproic acid and clonazepam are the most useful agents. In hyperekplexia, treatment is directed against the disabling tonic spasms, rather than jerks. Carbamazepine, phenytoin and clonazepam are useful agents in this respect. Ballistic overflow myoclonus may improve with anticholinergic drugs, such as benzatropine (benztropine) or trihexyphenidyl (benzhexol). Antiepileptic drugs are disappointingly ineffective in this condition.

Treatment of palatal myoclonus is often unsuccessful, but phenytoin, carbam-
azepine, clonazepam, trihexyphenidyl and baclofen have been effective in some patients. Clonazepam is effective in over half of patients with propriospinal myoclonus, but other anticonvulsants are usually unhelpful. Segmental spinal myoclonus is often resistant to drug treatment, but diazepam, carbamazepine, tetrabenazine and, particularly, clonazepam are sometimes effective.

Myoclonus is defined as shock-like involuntary movements arising from the CNS. Most often these are due to brief bursts of muscle activity, resulting in positive myoclonus. Myoclonic jerks, however, may also result from sudden short inhibitions of ongoing tonic muscle activity, termed negative myoclonus. Myoclonus may be physiological or due to a variety of hereditary or acquired conditions. While myoclonus is often seen as part of an epileptic syndrome, this review focuses on those entities in which myoclonus dominates the clinical picture and is the major cause of disability.

Whenever possible, the underlying cause of the myoclonus should be identified and treated. Table I provides an aetiological classification of myoclonus. In practice, an accurate diagnosis cannot always be made, and some patients will be characterised syndromically, as, for example, in progressive myoclonic ataxia,[1] progressive myoclonic epilepsy[1] or spinal myoclonus.[2] In addition, only a few of the underlying causes of myoclonus are correctable, and in most cases treatment is symptomatic. Aetiological classifications have not proven very useful in predicting the response to drugs. However, electrophysiological investigations have been able to distinguish several different pathophysiological mechanisms (see table II) which have therapeutic implications. There have been a number of advances in our understanding of the physiology of different forms of myoclonus, and aspects of treatment are considered in the light of these findings.

1. Cortical Myoclonus

1.1 Physiological Basis

Cortical myoclonus is the result of an abnormal discharge in the sensorimotor cortex and rapidly conducting corticospinal pathways. It may consist of reflex myoclonus or jerks elicited by voluntary action. Both movement disorders are characterised by brief bursts of electromyographic (EMG) activity. This activity is preceded by pathological enlargement of the cortical components of the sensory-evoked response in reflex jerks, and a short-latency time-locked cortical correlate in the electroencephalogram (EEG) in action myoclonus. Cortical myoclonus may be focal, as with vascular and neoplastic cortical lesions, or multifocal. In the latter instance, the encephalopathy may be static, as in post-hypoxic encephalopathy, or progressive, as in the syndromes of progressive myoclonic ataxia and progressive myoclonic epilepsy.

This is the classical view of cortical myoclonus. However, over the last few years 2 further physiological abnormalities have been identified which, when present, contribute to disability. The first of these is the presence of both positive and negative myoclonus in some patients. In the latter, a brief silencing of muscle activity occurs which is cortical in origin. This results in sudden lapses in posture, particularly noticeable during gait, and tends to be more resistant to drug treatment than positive reflex or action myoclonus. The second abnormality consists of the spread of myoclonic activity within and between the sensorimotor cortices in some patients, so that bilateral or generalised jerks result.[3]

Cortical myoclonus results from increased cortical excitability, as witnessed by giant evoked potentials, cortical correlates and the pathological spread of activity within and between the sensorimotor cortices. In addition, cortical inhibitory processes, which would normally keep excitation in check, are deficient. This can be shown in vivo using the technique of transcutaneous stimulation of the motor cortex. A conditioning magnetic shock to either the ipsilateral or contralateral motor cor-