Prevention and Management of Drug-Induced Peripheral Neuropathy

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Summary

When symptoms of peripheral neuropathy appear, the possibility that they have been induced by drugs should be considered. A large number of drugs of all kinds, several of which are considered indispensable, have been implicated in peripheral neuropathy. A list of some of these drugs is provided. Neuropathy is a universal and dose-limiting factor during treatment with vinca alkaloids, but is otherwise a rare complication of drug therapy. Drug-induced peripheral neuropathy is almost always due to a dose-dependent primary axonal degeneration caused either by toxic reactions or by metabolic changes in neurons or their surroundings. The use of drugs should be restricted, especially in patients with a risk for development of neuropathy or with already existing neuropathy, e.g. patients with hepatic or renal failure, diabetes mellitus, or malnutrition. Patients should be given vitamins, prophylactically or therapeutically, which will sometimes allow a treatment to be continued. In other cases of drug-induced neuropathy the drug should be stopped. Reversal depends on the severity of the neuropathy, intensity and duration of the treatment and existence of causative cofactors, but generally the prognosis is good. While waiting for recovery physiotherapy is of importance, and when paraesthesia and pain are troublesome the patient should be treated with carbamazepine, imipramine or lidocaine (lignocaine).
Peripheral neuropathy is a general term referring to any disorder (infectious, toxic or metabolic) that affects peripheral nerves. The neuropathic effects may be either motor, sensory, sensorimotor or autonomic, or any combination thereof. The fact that many neuropathic agents may give rise to disabling and sometimes irreversible change to the nervous system stresses the significance of prevention, recognition and restriction.

This article aims to offer information on the prevention and management of iatrogenic, drug-induced peripheral neuropathy, which is almost always reversible when the drug is withdrawn in good time.

New drugs are constantly being introduced, and likewise constantly identified as causes of peripheral neuropathy. It is not possible to supply a complete list of the agents which give rise to this problem in humans; the number is certainly impressive. In any case of neuropathy, the possibility that it is drug-induced should be considered.

1. The Peripheral Nervous System

The peripheral nervous system consists of motor, autonomic and sensory neurons together with Schwann cells, and comprises nerves outside the central nervous system. It therefore includes the dorsal and ventral spinal roots, cranial and spinal nerves and the major parts of the autonomic system (Thomas 1984).

2. Peripheral Neuropathy

Two major anatomical categories of peripheral neuropathy can be distinguished:

1. Polyneuropathy, defined as clinical syndromes resulting from widespread symmetrical affliction of the peripheral motor and/or sensory neuron.
2. Mononeuropathy, due to focal lesions of peripheral nerves (Thomas 1984). These neuropathies are relatively uncommon.

Table I is a modified version of the classification proposed by Schaumburg et al. (1986).

2.1 Pathogenesis

The exact pathogenesis and the pathophysiological mechanism underlying neuropathy are not known, although it is unlikely that any single factor can explain all neuropathies. At present various mechanisms including genetic, toxic, metabolic, vascular, immunological or inflammatory mechanisms are assumed to play a role (Asbury & Gilliatt 1984; Schaumburg et al. 1986; Thomas 1984).

In distal axonopathy the primary event is a metabolic abnormality that affects the axonal transport, causing degeneration of long and large diameter motor and sensory axons. The degeneration gradually moves proximally (dying back) towards the nerve cell body. Axonal disintegration may be followed by a secondary demyelination (Spencer & Schaumburg 1984).

In myelinopathies the initial lesion is limited to Schwann cells and myelin, while axons are spared. In acute inflammatory demyelinating polyradiculoneuropathy (Guillain-Barré syndrome), the prototype of a myelinopathy, demyelination is assumed to be due to an immune-mediated lesion of the myelin. Following the initial demyelination the remaining Schwann cells divide and remyelinate denuded axons, forming short internodes (Dyck et al. 1984; Windebank & Dyck 1984).

In neuronopathies the primary lesion is confined to neuronal cell bodies and includes a variety of neuropathic disorders with involvement of motor, sensory and autonomic cell bodies. Dorsal root ganglion cells are assumed to be particularly vulnerable to some circulating toxins: following their degeneration, Schwann cells remain and the axons fail to regenerate.

In focal neuropathy various mechanisms such as ischaemia, infiltration and injury may affect and interfere with axonal metabolism and myelination. In injuries 3 different types of lesions are seen, the character depending on the severity of the injury. In the less severe form the result is a neuropraxia